

INTESTINAL ARTERIES

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FIFTY-SIX FIGURES

GENERAL CONSIDERATIONS

The following study was undertaken as a means to obtain information regarding the degree of viability of the intestine subjected to various types of traumatism. Clinically, there is a marked factor of safety in the return of the circulation to a strangulated segment or loop of intestine. Intestinal anastomosis following resection usually heals readily, as do wounds of the gut and mesentery when sutured. Unfortunately, a number of fatalities occur as the result of gangrene of a strangulated loop of gut, in which the circulation apparently returns at the time of operation, but subsequently becomes impaired. In numerous instances leakage follows the repair of an intestinal anastomosis, the result of a small area of necrosis at the site of the anastomosis. Occasionally, gangrene of the bowel follows the repair of mesenteric rents. Can these varying results be explained in part, at least, by any special arrangement of the arteries at the mesenteric border and within the coats of the intestine?

In 1897 and 1903 Dwight made a careful study of the mesenteric arteries and the vasa recta passing from the last series of mesenteric arterial arcades to the intestine. His description of the arrangement of the arteries in the mesentery was the first complete report to appear in the literature. Monks, in 1903, in an excellent description of a means to determine the localization and direction of a loop of bowel

presenting from an abdominal incision, also described the mesenteric arteries and vasa recta in detail. The course of the vasa recta is portrayed in a general way in Ferguson's ('05) text-book of histology. The circulation of the villus is depicted and illustrated by Mall ('87). In the literature reviewed no minute study of the arrangement and relationship of the arteries to the various coats of the intestine has been found. Furthermore, no differences in the disposition of the arteries in various parts of the large and small intestine have been noted, except in a general way. The arteries at the mesenteric border which are so important technically in various surgical procedures are dismissed with a few words.

I take this opportunity of thanking Prof. H. D. Senior for valuable suggestions and criticism; Miss H. L. Hubbinger for aid in the preparation of the cleared injected specimens, and Mr. F. Peterson for his interest in the preparation of the illustrations. I am greatly indebted to Drs. C. Norris, T. Gonzales, and C. Darlington for their generosity in placing fresh material at my disposal.

MATERIAL

In the present investigation, fresh, dissection, and cleared injected specimens (Spalteholz method, '11) have been studied. Corrosion preparations prepared according to the method of Hinman et al ('23) did not provide a satisfactory method of study of the intestinal arteries within the wall of the gut, as the relationship to the various coats of the intestine was necessarily lost. Special attention has been given to segments of gut in the duodenum,¹ oral jejunum, aboral jejunum, oral ileum, aboral ileum, and colon. Comparative observations were made of similar locations in human, both adult and infantile, intestines, and in the intestine

¹ The special segments under consideration are designated as duodenum, oral jejunum, aboral jejunum, oral ileum, aboral ileum, and colon, as suggested by Hertzler ('19) as being a more convenient method of expression than units of distance as employed by Monks.

of the adult dog. The cleared specimens were examined through the binocular microscope.

DESCRIPTION OF INTESTINAL ARTERIES

At the mesenteric border pairs of vasa recta arise from the last series of mesenteric arcades and pass directly to the intestine (fig. 1f). These arteries generally come off sepa-

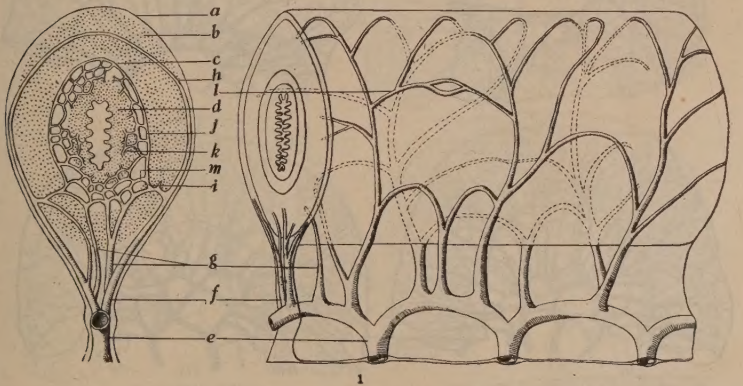
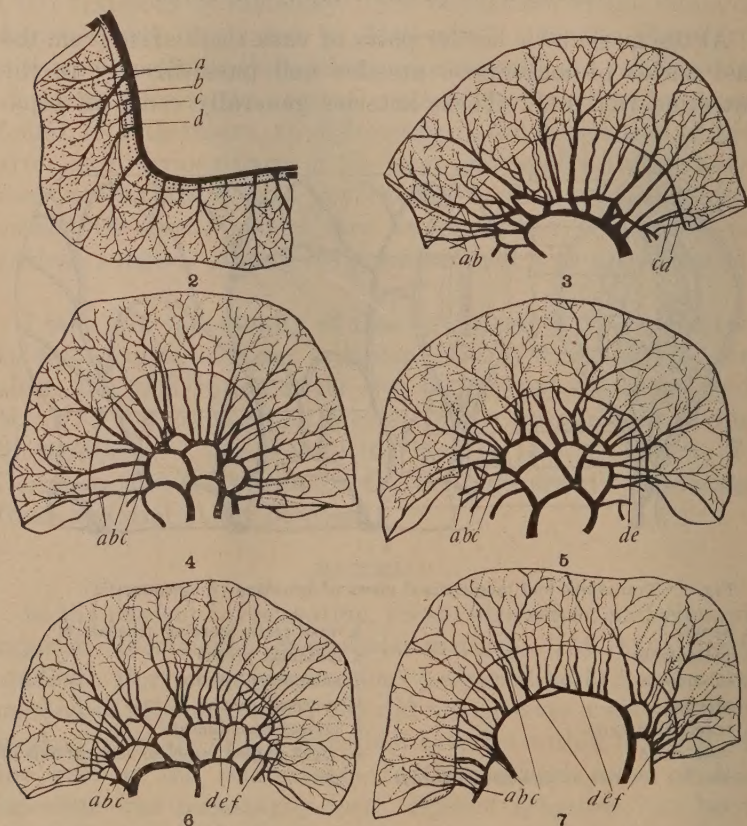


Fig. 1 Transverse and longitudinal views of intestine (diagrammatic).

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| <i>a</i> , serosa | <i>h</i> , vasa recta piercing muscularis |
| <i>b</i> , muscularis | <i>i</i> , muscular plexus |
| <i>c</i> , submucosa | <i>j</i> , submucosal plexus |
| <i>d</i> , mucosa | <i>k</i> , mucosal plexus |
| <i>e</i> , terminal arcade | <i>l</i> , lateral anastomosis |
| <i>f</i> , vasa recta | <i>m</i> , right-angled vessel to vertical axis of |
| <i>g</i> , smaller arteries at mesenteric border | gut |

rately and alternate, one passing in front of, the other behind the intestine, as described by Dwight and Monks (fig. 1). However, they appeared in numerous instances as a single vessel in profile, being recognizable as a pair only when separated by moving the leaves of the mesentery (fig. 1f). In a few cases they arise as a single vessel and divide into two, three, or four arteries (fig. 5 a, b, c), alternating singly or in pairs.

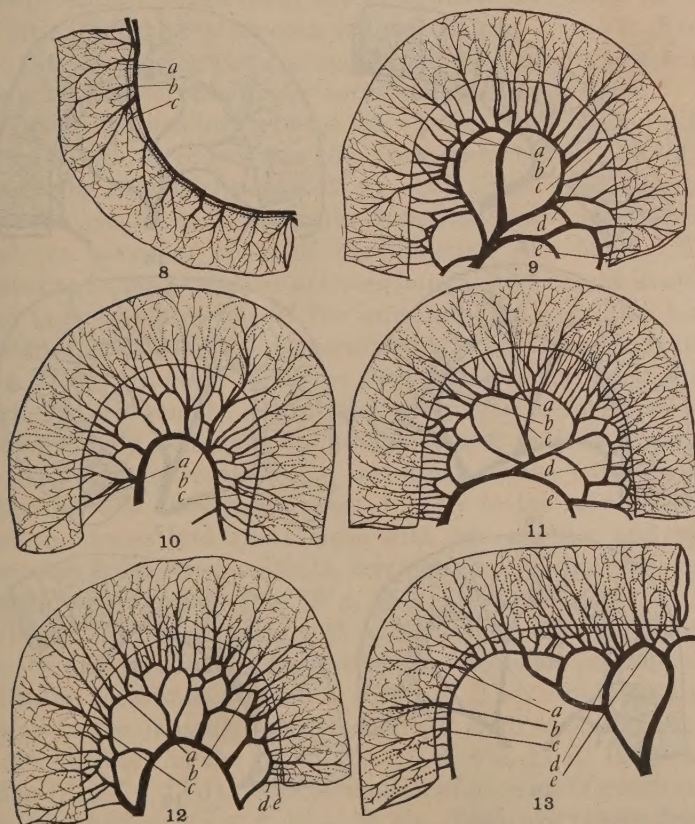
In the duodenum (figs. 2 a, 8 a) and oral jejunum (figs. 3 a, 9 a) the vasa recta alternate and in a few instances occur as double vessels (figs. 2 b, 8 b, 3 b, 9 b). Bifurcation (figs. 3 c,



Figs. 2 to 7 Adult intestine. 2, duodenum; 3, oral jejunum; 4, aboral jejunum; 5, oral ileum; 6, aboral ileum; 7, colon.

9 c) and three vessels (fig. 9 d) arising from a common stem are occasionally found. Upon approaching the oral ileum these branching vessels (figs. 4 a, b, 10 a, b) appear more frequently and are greatly increased in the ileum (figs. 5 a, b, c, 6 a, b, c, 11 a, b, c, 12 a, b) with a decrease of single

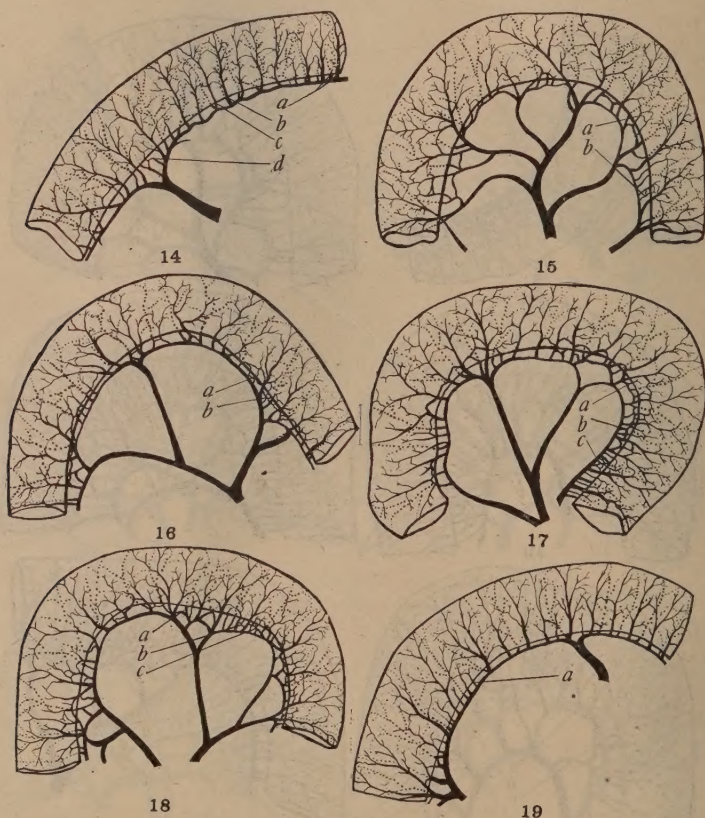
vessels (figs. 6 d, 12 c). The arrangement of the vasa recta in the colon (figs. 7 a, b, c, d, 13 a, b, c) is similar to that found in the duodenum and oral jejunum. A corresponding



Figs. 8 to 13 Infantile intestine. 8, duodenum; 9, oral jejunum; 10, aboral jejunum; 11, oral ileum; 12, aboral ileum; 13, colon.

distribution predominates throughout the intestine of the dog, namely, vasa recta which appear as single arteries and alternate (fig. 14 a); double arteries which appear as single (fig. 14 b) and those that bifurcate (fig. 14 c).

The vasa recta, in passing between the serosa and muscularis, give off numerous lateral off-shoots which unite with similar branches from adjacent arteries (fig. 11). The



Figs. 14 to 19 Canine intestine. 14, duodenum; 15, oral jejunum; 16, aboral jejunum; 17, oral ileum; 18, aboral ileum; 19, colon.

vasa recta pierce the muscular coat in the mesenteric quarters of the small intestine (fig. 21 a) and the antimesenteric quarters in the large intestine (fig. 31 a). They branch out in tree-like fashion as they approach the antimesenteric border (fig. 20 a) and anastomose freely with similar branches

of the arteries of the opposite side. Numerous branches are given off from the vasa recta at right angles to the vertical axis of the gut (figs. 1 m, 56 j). These branches in turn divide and inosculate with similar branches above and below as well as laterally in the submucosa and mucosa (fig. 1 i, j, k). From the plexuses in the latter situation arteries arise which enter the villi (fig. 56 m), finally terminating in capillaries.

Numerous smaller arteries also arise from the terminal arcades and directly from the vasa recta before the latter reach the muscularis (fig. 1 g). At times small distinct arcades are found between the terminal mesenteric arcades and the muscular coats of the intestine (fig. 56 i). The branches from the smaller arteries inosculate with one another and pass to both sides of the intestine (fig. 1 g). In some instances they pierce the muscularis at the mesenteric border (fig. 23 a). In other instances these arteries run for a short distance between the serosa and muscularis before entering the latter (fig. 56 h) and do not anastomose until they ramify in the muscular coat of the intestine. After entering the muscular coat they pass almost directly to the submucosa in both instances and anastomose with one another and with branches from the vasa recta, completing a more or less concentric anastomosis (figs. 25 a, 56 h).

These smaller arteries with a formation of an occasional arcade are moderate in number in the duodenum of adult and infantile intestines (figs. 2 c, d, 8 c). They are sometimes found in the jejunum (figs. 3 d, 4 c, 9 e, 10 c) and occur in large numbers in the ileum (figs. 5 d, 6 e, 11 d, 12 d) and colon (figs. 7 e, 13 d). The formation of arcades is greatest in the ileum (figs. 5 e, 6 f, 11 e, 12 e). They are rarely found in the jejunum and are occasionally present in the colon (figs. 7 f, 13 e).

In the duodenum of the dog the smaller vessels are few in number (fig. 14 d); moderate in the jejunum (figs. 15 a, 16 a) and numerous in the ileum (figs. 17 a, 18 a) and colon (fig. 19 a). The arcades are absent in the duodenum and rarely do they occur in the colon. An occasional arcade is



Figures 20 to 55

found in the oral jejunum (fig. 15 b). They increase in numbers in the aboral jejunum (fig. 16 b) and are still more numerous in the ileum (figs. 17 b, 18 b) where secondary arcades make their appearance (figs. 17 c, 18 c). Further differentiations of intestinal arteries in human and canine intestines are shown in tables 1, 2, and 3 and are in accord with the findings of Dwight and Monks.

EXPERIMENTAL

In a previous communication ('24) experiments were reported which were performed to establish the relative margin of safety following the ligation of different vessels of the intestine in the dog. Since then a series of experiments has been carried out in which various vessels of the intestine were ligated and subsequently injected with a pigmented gelatin. The object of these experiments was to ascertain

20 to 55 Vasa recta and smaller mesenteric border vessels, longitudinal and transverse sections. Binocular study of cleared specimens.

Adult

20 longitudinal section, duodenum	26 longitudinal section, oral ileum
21 transverse section, duodenum	27 transverse section, oral ileum
22 longitudinal section, oral jejunum	28 longitudinal section, aboral ileum
23 transverse section, oral jejunum	29 transverse section, aboral ileum
24 longitudinal section, aboral jejunum	30 longitudinal section, colon
25 transverse section, aboral jejunum	31 transverse section, colon

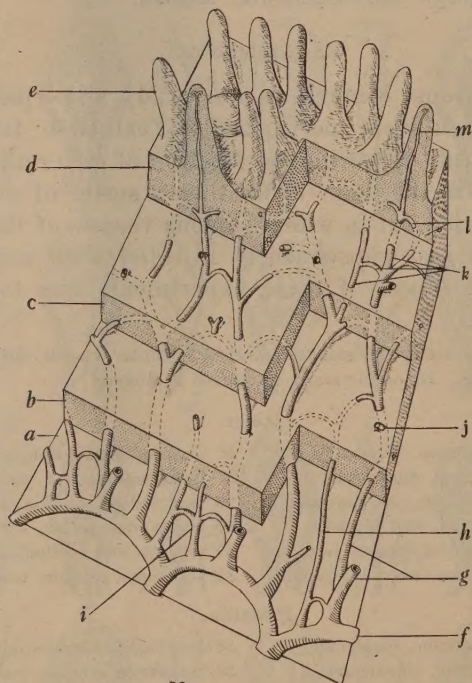
Infantile

32 longitudinal section, duodenum	38 longitudinal section, oral ileum
33 transverse section, duodenum	39 transverse section, oral ileum
34 longitudinal section, oral jejunum	40 longitudinal section, aboral ileum
35 transverse section, oral jejunum	41 transverse section, aboral ileum
36 longitudinal section, aboral jejunum	42 longitudinal section, colon
37 transverse section, aboral jejunum	43 transverse section, colon

Canine

44 longitudinal section, duodenum	50 longitudinal section, oral ileum
45 transverse section, duodenum	51 transverse section, oral ileum
46 longitudinal section, oral jejunum	52 longitudinal section, aboral ileum
47 transverse section, oral jejunum	53 transverse section, aboral ileum
48 longitudinal section, aboral jejunum	54 longitudinal section, colon
49 transverse section, aboral jejunum	55 transverse section, colon

whether there was any difference between the expected factor of safety by injection and the actual factor as brought out by operating upon living animals. The results of the injection experiments are detailed in table 4. In table 5 they are compared with those previously obtained on experimental animals.



56

Fig. 56 Reconstruction of human intestine showing relationship of arteries to intestinal coats (diagrammatic).

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| <i>a</i> , serosa | <i>i</i> , anastomosis of smaller arteries at mesenteric border |
| <i>b</i> , muscularis | <i>j</i> , right-angled vessel to vertical axis of gut |
| <i>c</i> , submucosa | <i>k</i> , submucosal plexus |
| <i>d</i> , mucosa | <i>l</i> , mucosal plexus |
| <i>e</i> , villus | <i>m</i> , artery to villus |
| <i>f</i> , terminal arcade | |
| <i>g</i> , vasa recta | |
| <i>h</i> , smaller arteries at mesenteric border | |

TABLE 1

Observations made upon intestinal arteries in adult intestine (twenty-six cadavers)

LOCATION	MESENTERIC ARTERIES	No. to 5 cm.	VASA RECTA		SMALL ARTERIES MESENTERIC BORDER
	No. of arcades		Length arcade to m.b.	Origin from terminal arcades and relation to intestine	
Duodenum	occasional first	14	1½-3 cm.	single alternate-double as single-bifurcate as single	moderate main vessel, few vasa recta, occasional arcade
Oral jejunum	first-majority second-occasional third	20	3-3½ cm.	single alternate majority - rarely bifurcate-occasional three common stem	few terminal arcades and vasa recta, occasional arcade
Aboral jejunum	first-second-majority third-occasional fourth	22	3-3¼ cm.	single alternate-double as single-bifurcation increased	few terminal arcades and vasa recta, occasional arcade
Oral ileum	first-second-majority third-occasional fourth-plexus formation	31	2-3 cm.	single alternate-double as single-bifurcate alternate	numerous terminal arcades and vasa recta, few arcades
Aboral ileum	first-second-third-fourth-fifth-plexus formation	30	1-2½ cm.	single alternate-double as single-three to four common stem alternate	numerous terminal arcades and vasa recta, moderate arcades well defined
Colon	none-first second occasional third at flexures	18	½-1 cm.	single alternate majority-bifurcate as single-double as single	numerous main vessel terminal arcades at flexures and vasa recta, occasional arcade

m.b., mesenteric border.

TABLE 2

Observations made upon intestinal arteries in infantile intestine (seven cadavers)

LOCATION	MESENTERIC ARTERIES	VASA RECTA		SMALL ARTERIES MESENTERIC BORDER	
	No. of arcades	No. to 5 cm.	Length arcade to m.b.	Origin from terminal arcades and relation to intestine	
Duodenum	occasional first	22	3 mm.	single alternate-double as single-bifurcate as single-rarely three to stem	moderate main vessel few vasa recta, occasional arcade
Oral jejunum	first-majority second-occasional third	30	1 cm.	single alternate majority-double as single-bifurcate as single-occasional three to stem two front one behind	few terminal arcades and vasa recta, occasional arcade
Aboral jejunum	first-second-majority third	28	1 cm.	bifurcate alternate-three to four common stem alternate two and one, two and two-occasional double as single and single alternate	moderate terminal arcades few vasa recta, occasional arcade
Oral ileum	first-second-third-occasional fourth-fifth-plexus formation	37	3 mm.	bifurcate alternate-three to four common stem alternate two and one, two and two-occasional double as single and single alternate	numerous terminal arcades and vasa recta, few arcades
Aboral ileum	first-second-third-fourth-occasional fifth-plexus formation	36	2 mm.	bifurcate as single majority-occasional single alternate-double as single-three to four common stem alternate	numerous terminal arcades and vasa recta, moderate arcades
Colon	none-first-second-occasional third at flexures	20	1-2 mm.	single alternate-double as single-bifurcate as single	numerous main vessel terminal arcades at flexures few vasa recta, few arcades

m.b., mesenteric border.

TABLE 3

Observations made upon intestinal arteries in canine intestine (twenty animals)

LOCATION	MESENTERIC ARTERIES	VASA RECTA		SMALL ARTERIES MESENTERIC BORDER	
	No. of arcades	No. to 5 cm.	Length arcade to m.b.	Origin from terminal arcades and relation to intestine	
Duo- denum	none	15	3 mm.	double as single	few main vessel, no arcades
Oral jejunum	majority first- occasional second	19	4-6mm.	bifurcate as single majority- single alternate	moderate terminal arcades few vasa recta, few arcades
Aboral jejunum	majority first- more second- occasional third	26	2-6mm.	bifurcate as single majority- single alternate	moderate terminal arcades and vasa recta, moderate arcades
Oral ileum	majority first and second- occasional third	30	2-4mm.	double as single- single alternate- two to three common stem	numerous terminal arcades and vasa recta, moderate arcades, occasional second arcade
Aboral ileum	majority first and second- occasional third	32	1-3mm.	double as single- bifurcate as single	numerous terminal arcades and vasa recta, moderate arcades, occasional second arcade
Colon	none- occasional first- rarely second at flexures	16	3-6mm.	double as single majority- bifurcate as single	numerous terminal arcades few vasa recta, occasional arcade

m.b., mesenteric border.

TABLE 4

Showing the range of flow of injection fluid to the vasa recta after ligation of various vessels of the mesentery in the dog

EXPT. NO.	LOCATION AND VESSELS LIGATED	VESSELS INJECTED	RESULTS
6	Duodenum:		
7	a. pancreatico-duodenalis 8 contiguous vasa recta	a. pancreatico-duodenalis a. pancreatico-duodenalis	vasa recta N R vasa recta N R except at upper extreme 1 vessel
8	Oral jejunum: 2 contiguous first arcade	double at extremes of arcade	vasa recta R
9	2 contiguous second arcade including vasa recta at extremes (oblique ligation)	double at extremes of arcade	vasa recta N R
10	5 contiguous vasa recta	double at extremes of arcade	vasa recta N R except at upper extreme 1 vessel
12	Aboral jejunum: 2 contiguous second arcade	vessel of first arcade	vasa recta R
15	Oral ileum: 3 contiguous first arcade	aa. intestinalis.	vasa recta N R
16	1 vessel second arcade	vessel of first arcade	vasa recta R
17	3 vessels second arcade	vessel of first arcade	vasa recta R
18	3 contiguous vasa recta	vessel of first arcade	vasa recta N R
19	Aboral ileum: 1 vessel first arcade	contiguous vessel first arcade	vasa recta R
20	2 contiguous vasa recta	vessel of first arcade	vasa recta N R
21	4 contiguous vasa recta	vessel of first arcade	vasa recta N R
25	Colon: 3 contiguous vasa recta	a. colica sinistra	vasa recta N R except at lower extreme half of one vessel
26	3 alternating vasa recta	a. colica sinistra	vasa recta N R except for a few lateral branches

Vasa recta injected = R. Vasa recta not injected = N R.

In experiments nos. 7, 10, 25, 26, the partial and complete injection of the vasa recta indicated may be explained by the fact that the fluid flowed through the smaller arteries at the mesenteric border and the lateral branches of the contiguous injected vasa recta.

It appears from tables 4 and 5 that there is a greater factor of safety after ligation of vessels of the second arcade in the dog, as compared to ligation of other mesenteric vessels. This is readily explained upon an anatomical basis because of the free anastomosis existing around the ligatures.

TABLE 5

Showing the comparative results obtained after ligation of various mesenteric vessels in the return of the circulation to a segment of gut in experiments on dogs and the range of flow of injection fluid to the vasa recta

RESULTS OF ANIMAL EXPERIMENTS	VESSELS LIGATED	RESULTS OF INJECTION EXPERIMENTS
N R	aa. intestinalis	N R
R	primary arcade	R
N R	one vessel	R
N R	two vessels	N R
	three vessels	
	secondary arcade	
R	one vessel	R
R	two vessels	R
R	three vessels	R
N R	two vessels	N R
	(oblique ligation	
	including vasa recta	
	at extremes)	
R	vasa recta	R
R	one vessel	N R
R	two vessels	N R
R	three vessels	N R
N R	four vessels	N R
N R	five vessels	N R

Circulation returned = R.

Vasa recta injected = R.

Circulation did not return = N R.

Vasa recta not injected = N R.

The margin of safety with human intestine after the ligation or injury of similar vessels must necessarily be increased on account of the greater number of arcades. The factor of safety in both man and dog is greater in the jejunum and ileum than in the duodenum and colon, but in these latter locations the lack of mesenteric arcades is compensated for by the fixation of these parts of the intestinal canal.

CONCLUSIONS

1. The vasa recta encircle the intestine and their branches in anastomosing converge toward the lumen and also run more or less parallel to the longitudinal axis of the intestine.

2. There is a well-defined mesenteric border arterial anastomosis discernible in the cleared injected specimens in addition to the vasa recta.

3. The factor of safety in the dog is greater following ligation of the vessels of the secondary mesenteric arcade than after that of any other part of the mesenteric circulation.

4. The factor of safety in the dog is less following ligation of the vessels of the first arcade or vasa recta and nil following ligation of the aa. intestinalis.

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SOME POINTS IN THE REGIONAL ANATOMY OF THE OPTIC PATHWAY, WITH ESPECIAL REFERENCE TO TUMORS OF THE HYPOPHYSIS CEREBRI AND RESULTING OCULAR CHANGES

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SEVENTEEN FIGURES

Clinical observations show that certain ocular changes constitute one of the chief and earliest symptoms in a large number of tumors of the hypophysis cerebri. Indeed, it would appear that the ocular manifestations occasionally are the only means of a preoperative diagnosis at a relatively early time of the disease. The early eye changes appear to antedate the constitutional symptoms. Perhaps, however, this is only apparent and not real and due to the greater precision now possible in detecting the earliest eye manifestations.

The ocular changes associated with hypophysial tumors consist in contracted fields, lessened visual acuity, and altered nerve heads. Typically, it would appear that the visual fields are progressively and characteristically bitemporally distorted and that the nerve heads show fairly constant and characteristic changes.

DeSchweinitz and Carpenter, in a contribution as early as 1905, direct attention to a number of lesions which may produce alterations in the structure and function of the optic chiasm. They point out that in the presence of a typical bilateral hemianopsia, which may be regarded as the localizing form of hemianopsia, it is practically impossible to make a mistake, and the lesion must necessarily be one which destroys the conductivity of the crossed fasciculi. Finally, the fact that

a scotoma may be the beginning of a visual-field defect which will eventuate in a bitemporal hemianopsia and be significant of chiasm disease should not be forgotten, and, moreover, a scotoma which to careless examination would seem to indicate simply papillomacular bundle involvement and not involvement of the intermingling of the papillomacular fibers in the chiasm.

Benedict says: "Pallor of the discs and changes in the visual fields should always incite suspicion of pressure processes the etiology of which should be ascribed less hastily to tabes and other neuritic processes." Cushing and Walker state that primitive distortions are wanting in nearly half of the examples of hypophysial disease in the stage at which they are commonly recognized to-day ('14-'15); and in the second place, that in about 20 per cent of the patients actually showing characteristic neighborhood symptoms¹ there occurs no perimetric change demonstrable by our present methods ('14-'15). From the latter they infer that the chiasmal fibers are capable of considerable distortion by a growth in the neighborhood without a demonstrable encroachment upon the fields of vision. Lillie recently encountered four patients in which the ocular changes could not be distinguished from those characteristic of a pituitary syndrome. He, however, thinks a careful examination of the fields early in the course of the disease might have led to a correct preoperative diagnosis. Cushing and Walker hold that "the conclusion that an existent clean-cut bitemporal hemianopsia is an evidence of a medial lesion, most often due to a tumefaction of the hypophysis or its stalk is justifiable enough; but the reverse argument does not hold—that the absence of this characteristic defect or indeed of any defect whatsoever in the fields, necessarily speaks against a primary or interpeduncular growth." The latter authors found four groups of ocular changes in hypophysial tumors; the bitemporal, the homonymous, the amaurotic (blind in one or both eyes on

¹ Pressure on neighboring structures, optic chiasma, oculomotor nerve, olfactory tracts, uncinate gyri, *cura cerebri*, etc., giving rise to symptoms and signs.

admission), and the unclassified in which bizarre fields accompanied known hypophysial lesions. Traquair urges the importance of critically comparing field changes in cases due to a variety of causes and of uniformity in method. He found in attempting to study the relation of the field defects to the underlying causal condition that little help is obtained from the literature.

PRESENT INVESTIGATION

Our knowledge of the production of ocular changes in disorders of the hypophysis cerebri is, unfortunately, still defective. With the thought that a restudy of the relational anatomy of the parts concerned might emphasize certain more or less established facts and possibly bring some new factors to bear on the problem, the present investigation was undertaken in collaboration with Professor deSchweinitz.²

At the outset of the study it became apparent that too close adherence to a conventional, ideal, or text-book anatomy has befogged much that has been written on the relation between the ocular changes and hypophysial and certain other conditions. The query presented itself whether or not anatomic variations from the so-called normal possibly could account for some hitherto unexplained conditions and whether or not a more or less stable anatomy underlies certain of the more constant and progressive eye manifestations in hypophysial tumors and affections of the paranasal sinuses.

THE SUPERIOR SURFACE OF THE BODY OF THE SPHENOID BONE

Developmental factors

It would be superfluous in this connection to enter into details concerning the embryology of the sphenoid bone. However, certain points appear to be applicable and apropos.

² The reader is referred to the Bowman Lecture, 1923, by Prof. G. E. deSchweinitz, in which reference is made to some of the anatomical phases of the study. Moreover, an extensive consideration of the clinical aspects is presented. The figures presented herewith, save figure 7, are adapted from the Bowman Lecture, 1923, London: Adlard & Son & West Newman, Ltd., 23, Bartholomew Close, E. C. 1.

Briefly stated for purposes here, the sphenoid bone is ossified in four principal portions, corresponding to the presphenoid proper, orbitosphenoids, postsphenoid proper, and alisphenoids, a fifth independent element forming the medial pterygoid plate. The postsphenoid is formed from two pairs of ossific centers, a medial pair which fuse in the formation of the walls of the fossa hypophyseos (sella turcica) and related parts and a lateral pair for the alisphenoids or great wings. The presphenoid also has two pairs of centers, a lateral pair external to the optic foramina for the orbitosphenoids or small wings and a medial pair internal to the optic foramina which together form the anterior portion of the sphenoidal body. The small wings are at first attached by two roots to the lateral sides of the presphenoid, but after a time the anterosuperior root of the two sides grows over the upper surface of the presphenoid, which previously was exposed between the orbitosphenoids (small wings). These roots, of the two sides, fuse in the midplane, forming the jugum sphenoidale, covering to a greater or less extent the cranial surface of the presphenoid proper. This leads to the smooth expanse of bone in the anterior cranial fossa in front of the so-called chiasmatic sulcus.

The posterior edge of the fused anterosuperior roots of the small wings over the presphenoid forms the limbus sphenoidalis; variously differentiated in the adult; now very prominent, again less so, or absent altogether, as such. Typically, there remains an area of the cranial surface of the presphenoid behind the overlapping anterosuperior roots of the lesser wings. This area participates in forming the floor of the anterior cranial fossa and becomes the so-called sulcus chiasmatis; the width of which is more or less dependent on the encroachment by the lesser wings, and the plane of direction of the sulcus largely due to the degree of vertical growth of the hindmost portion of the presphenoid.

The pre- and postsphenoids proper fuse, forming a variable elevation, the tuberculum sellae, behind the sulcus chiasmatis and in front of the fossa hypophyseos, the line of junction.

The sphenoidal sinus arises in connection with the posterior cupola of the cartilaginous nasal capsule and variously pneumatizes the body of the sphenoid bone. However, it would carry us too far afield to discuss the development of the paranasal sinuses here. Reference will be made later and only where applicable.

Adult anatomy

Typically, the superior surface of the body of the sphenoid presents a variable transverse groove, the chiasmatic sulcus or the optic groove, which terminates on each side in the optic foramen, and is limited anteriorly by the limbus sphenoidalis and dorsally by the tuberculum sellae or olivary eminence. The sulcus or groove varies from a relatively wide surface to a total absence as such. Usually it is placed either in a horizontal plane or is directed slantingly at various degrees, looking toward the hypophysial fossa or sella turcica. Occasionally the hindmost portion of the presphenoid develops but little, if any, in height, with the result that the chiasmatic sulcus is placed in the vertical plane, and in a sense represents the posterior surface of the anterior portion of the presphenoid proper augmented by the dorsal border of the overlapping roots of the small wings. In these cases, the sphenoidal limbus forms an upper instead of an anterior border of the chiasmatic sulcus. This usually means a lowered position of the optic foramina. Correspondingly, the optic chiasma is much closer to the diaphragma sellae and occasionally by its anterior border (not basal surface) is brought in contact with the dorsal wall of the sphenoidal sinus—an important clinical fact to which reference will be made later.

Behind the chiasmatic sulcus when in the horizontal or oblique plane, and below it when in the vertical plane, is the tuberculum sellae or olivary eminence. Laterally from the tuberculum project the inconstant middle clinoid processes and immediately behind is the hypophysial fossa (sella turcica), the posterior boundary of which is a quadrilateral

plate of bone, the dorsum sellae (dorsum ephippi), from which project the posterior clinoid processes, more or less overhanging the hypophysial fossa. The same is frequently true of the dorsum sellae proper. The separate chondrification of the posterior clinoid processes probably accounts for their occasional absence.

THE LOCATION OF THE OPTIC CHIASMA

At first thought it may appear strange that so important and conspicuous a structure as the optic chiasma should be subject to gross misstatements concerning its location. However, this may, in a measure, be due to the fact that the chiasma is more usually observed on brains after their removal from the skull cavity. Of course, this gives no evidence of relations at the base of the skull. Another pitfall is the naming of the transverse groove behind the sphenoidal limbus of the superior surface of the body of the sphenoid the chiasmatic sulcus. This designation is a misnomer, since only rarely does the optic chiasma bear close relationship to the chiasmatic sulcus. Because of the name, apparently, it is assumed that the chiasmatic sulcus lodges the optic chiasma. Again, errors are carried from book to book and from book to verbal discussions.

It may not be amiss to quote from a few modern text-books: "Behind the jugum sphenoidale at the anterior margin of the sella turcica, there is a shallow groove, the optic groove (sulcus chiasmatis), so called because it contains the decussation or chiasma of the optic nerves," (Sobotta-McMurrich). "In front of the fossa (hypophysial fossa) is an elevated portion of bone on a level with the optic foramina, the tuberculum sellae, on which the optic commissure rests in the slight sulcus chiasmatis" (Quain's *Elements of Anatomy*, 11th ed.). Such descriptions are not based upon observation and are very misleading. Another text-book says: "This groove is liable to considerable variations and apparently does not always serve for the lodgment of the optic chiasma" (Cunningham's *Anatomy* [quoting Lawrence],

Rev. 4th ed.). Again, “. . . . above and behind which (the chiasmatic sulcus) lies the optic commissure” (Morris’ Human Anatomy, 6th ed.).

Lawrence observed a few specimens in which the commonly accepted position of the optic chiasma upon the chiasmatic sulcus was departed from. Unfortunately, he had opportunity to examine too few bodies to make his contributions of much value. However, he ventured the belief that an extended study would show that never is the optic chiasma lodged in the chiasmatic sulcus. This prophecy is near the truth. Zander, in a series of cases, showed that the posterior edge of the optic chiasma projects behind the dorsum sellae to the average of 1.58 mm. He found but few cases in which the posterior border of the chiasma lay in front of the dorsum sellae. Wallis found one case in ten in which more than one-half of the sagittal diameter of the optic chiasma lay upon the chiasmatic sulcus. The series again is too small and the percentage of optic chiasma related to the chiasmatic sulcus, therefore, too high as would appear by an examination of a larger series (*vide infra*). Fawcett, in speaking of the origin and intracranial course of the ophthalmic artery, directs attention to the position of the chiasma and confirms Lawrence’s earlier observation. Schaeffer, working on an entirely different problem, found that “the location of the optic commissure immediately over the hypophysis cerebri is very common according to the cadavers investigated.” However, the study was not made with reference to the points primarily raised in this connection.

MATERIAL AND FIELD OF INVESTIGATION

Between July, 1922, and February, 1923, the writer personally made observation and study of 125 freshly exposed brains on bodies soon after delivery to the Daniel Baugh Institute of Anatomy of the Jefferson Medical College of Philadelphia for scientific purposes. A series of measurements and observations were variously made in the bodies studied. These included, among others, the size and shape of the hypophysial

fossa; the width of the chiasmatic sulcus; the intracranial length of the optic nerves; the distances between the anterior border of the optic chiasma and the limbus sphenoidalis and the tuberculum sellae; the sagittal (anteroposterior) and the frontal (transverse) diameters of the optic chiasma; the relations and contacts of the basal surface of the optic chiasma; the distance between the diaphragma sellae and the basal surface of the optic chiasma; the direction and relation of the infundibulum; the character of the diaphragma sellae and its aperture; the chiasmatic cistern; the shape and plane of direction of the chiasmatic sulcus; the sphenoidal sinus and posterior ethmoidal cells; the canalicular segment of the optic nerve; the neighborhood arteries, etc.

Limited space forbids detailed discussion of all these observations and measurements. Therefore, some of them have been tabulated so as to conserve space and be more available for ready reference. However, some observations and measurements merit discussion under general headings.

POSITION OF THE OPTIC CHIASMA IN RELATION TO THE SPHENOIDAL SINUS AND POSTETHMOIDAL LABYRINTH

It is a significant fact and of great clinical import that in only five of the 125 bodies was the optic chiasma located far enough forward to make possible a frank relationship between the basal surface of the chiasma and the chiasmatic sulcus. And in these five cases not one was found wholly resting upon the chiasmatic sulcus, the remaining portion of the chiasma projecting backward for a greater or less distance over the sella diaphragm.

The observation, that in but 5 per cent of the examined bodies did the optic chiasma come into intimate relationship with the groove or sulcus named for it, namely, the chiasmatic sulcus, is almost unbelievable. Yet such was the case in the present series of bodies.

However, while the above statement is correct so far as the basal surface of the optic chiasma is concerned in its relation to a horizontal or oblique chiasmatic sulcus, the roof

of the sphenoidal sinus and certain posterior ethmoidal cells, it is misleading in that it does not take into account the instances in which the anterior border of the optic chiasma comes in contact with a vertically directed chiasmatic sulcus, or if not a chiasmatic sulcus, with a sheer vertical wall dropping off from the sphenoidal limbus. Mention was made of this anatomic type elsewhere. It is of great clinical significance; first, because of its location and, second, because it may be a factor in bitemporal hemianopsia, secondary to infection of the sphenoidal sinus. The optic chiasma in these cases comes in contact with the posterior wall of the sphenoid sinuses just above the diaphragma sellae and the underlying hypophysis cerebri. In this position it is in great hazard in hypophysial operations by the intranasal route. The distance in these cases between the sphenoidal limbus and the point of union between the pre- and postsphenoid is a considerable one, forming a goodly portion of the posterior wall of the sphenoidal sinuses. The only way to safeguard the optic chiasma in operations upon the hypophysis cerebri with such a relational anatomy is to make the approach to the hypophysial fossa as low as possible. Since the operator has no way of knowing whether or not this anatomic type confronts him, the intranasal approach should always be as low as feasible.

When the basal surface of the optic chiasm rests in part upon the chiasmatic sulcus, it usually bears a very intimate and vital relationship to the roof of the sphenoidal sinuses and often to certain posterior ethmoidal cells as well. Moreover, when those cases are added in which the anterior border of the chiasma comes in contact with a vertically directed chiasmatic sulcus, the 5 per cent of chiasma-paranasal-sinus contacts is increased accordingly.

BITEMPORAL AND TEMPORAL CHANGES IN PARANASAL SINUS CONDITIONS

If one can be guided by case reports, bitemporal hemianopsia, a condition in which the chiasmal fibers are involved,

is unusual in disease of the sphenoidal sinus and post-ethmoidal cells. However, it does occur. Anatomically, it would appear possible, when the optic chiasma rests upon a horizontal or oblique chiasmatic sulcus and when the anterior border of the chiasma touches a vertically directed chiasmatic sulcus. In the former case, the basal surface of the chiasma comes into intimate anatomic relationship with the roof of the sphenoidal sinuses and often with the walls of certain posterior ethmoidal cells. In the latter, the anterior border of the chiasma comes into intimate anatomic relationship with the posterior wall of the sphenoidal sinuses—a relationship which would not be altered even though the hypophysis cerebri and the diaphragma were interposed between the basal surface of the chiasma and any sphenoidal sinuses which might have pneumatized beneath the hypophysial fossa.

As stated above, these anatomic types are uncommon, hence the rarity of bitemporal hemianopsia secondary to involvement of the sphenoidal sinuses and the postethmoidal labyrinth. On the other hand, temporal contraction of the visual fields in infection of these air chambers is relatively common. This, doubtless, is due to the very intimate anatomic relationships that usually exist between the optic nerve, the sphenoidal sinus and certain posterior cells. In this relation, the nasal side of the optic nerve is, as a rule, the more exposed to danger. The sphenoidal sinus alone may be the factor, or the sphenoidal sinus and certain of the posterior ethmoidal cells together; or again, the hindmost of the posterior ethmoidal cells alone. Owing to the very common asymmetry of the two sphenoidal sinuses, one or the other alone may come into intimate anatomic relationship with the optic nerves of both sides and occasionally the optic chiasma as well.

The relationship may be illustrated by dividing the optic nerve into sinus and non-sinus portions, using sinus portion to mean that segment of the nerve which is 2 mm. or less from the walls of certain of the paranasal sinuses. Usually some portion of the segment is in actual contact with the osseous

wall or the mucous membrane (when there is an osseous defect) of one of the posterior ethmoidal cells, of the sphenoidal sinus, or of both. The non-sinus segment is beyond the

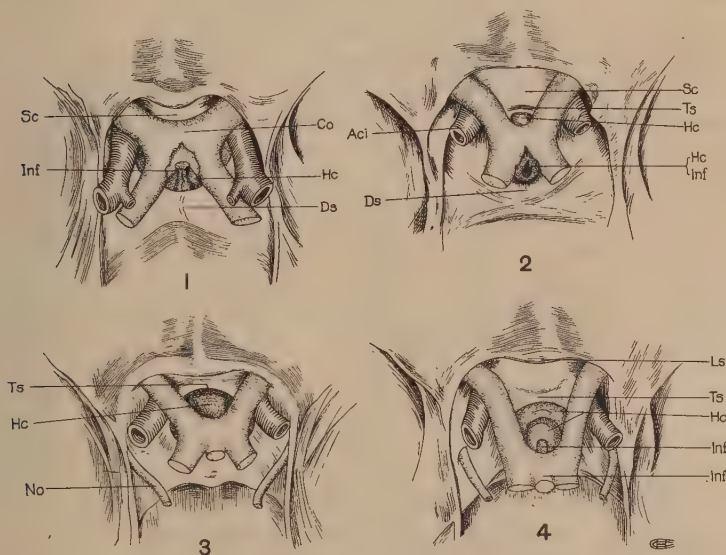


Fig. 1 Optic chiasma located in part on the chiasmatic sulcus, the remaining portion resting upon the diaphragma sellae. This type was found in 5 per cent of the bodies examined.

Fig. 2 Optic chiasma wholly located over the diaphragma sellae. This type was found in 12 per cent of the bodies examined.

Fig. 3 Optic chiasma almost wholly located over the diaphragma sellae, a small portion projecting on to the dorsum sellae. This type was found in 79 per cent of the bodies examined.

Fig. 4 Optic chiasma located on and behind the dorsum sellae. This type was found in 4 per cent of the bodies examined.

Sc, sulcus chiasmatis; *Inf*, infundibulum; *Co*, chiasma opticum; *Hc*, hypophysis cerebri; *Ds*, dorsum sellae; *Aci*, arteria carot. int.; *Ts*, tuberculum sellae; *No*, nervus oculomotorius; *Ls*, limbus sphenoidalis.

arbitrary 2-mm. limit and does not particularly concern us here. It has been observed that the farther removed the optic nerve is from the walls of diseased paranasal sinuses the less liable is the nerve to secondary involvement. The

appended table is illustrative of the lengths of the sinus and non-sinus portions of the optic nerve as compared with the total length of the nerve from the eyeball to the optic chiasma in a large series of cadavers investigated.

TABLE 1
Length of sinus and non-sinus portion of optic nerve

CADAVER	TOTAL LENGTH		NON-SINUS PORTION		SINUS PORTION	
	Right	Left	Right	Left	Right	Left
	mm.	mm.	mm.	mm.	mm.	mm.
1	45	45	24	21	21	24
2	37	35	14	13	23	22
3	44	44	21	22	23	22
4	40	40	19	23	21	17
5	55	48	28	27	27	21
6	43	41	15	15	28	26
7	48	46	24	20	24	26
8	39	42	15	14	24	28
9	38	40	16	20	22	20
10	40	40	30	10	20	20
11	37	36	14	14	23	22
12	54	48	28	27	26	21

POSITION OF THE OPTIC CHIASMA IN RELATION TO THE
DIAPHRAGMA AND HYPOPHYSIS

As stated elsewhere, in only five out of the 125 bodies did the optic chiasma occupy the chiasmatic sulcus and then only a portion of the chiasma was so located, the remaining portion projecting backward for a greater or less distance over the diaphragma sellae. Of the 120 chiasmata, in which no portion of the basal surface rested upon the tuberculum sellae and the chiasmatic sulcus, many more rested in small degree upon the dorsum sellae than were located in front of the latter, that is, wholly over the diaphragma sellae.³ Occasionally the chiasma was formed so far posteriorly that the whole of the basal surface of the chiasma rested upon and behind the dorsum sellae. On the other hand, in some the anterior border

³ The distance between the basal surface of the optic chiasma and the sella diaphragm varies greatly. The interval appears of sufficient clinical importance to justify a brief discussion of it in a subsequent paragraph.

of the chiasma touched or neared a vertically directed chiasmatic sulcus—an observation discussed previously.

For convenience and brevity, the measurements of the first twenty-five bodies examined are tabulated herewith, and since they are representative it would be superfluous to take up room with tables of the entire series. It will be noted that in but one of the twenty-five bodies (postmortem observation M) was the optic chiasma related to the chiasmatic sulcus, about half of its basal surface resting upon it. In four of the bodies (postmortem observations d, q, u, 237), there was a sheer vertical wall dropping from the sphenoidal limbus (the chiasmatic sulcus, in a sense, in the vertical plane, see elsewhere). In the latter, only the anterior border of the optic chiasma could possibly come into relationship with the modified chiasmatic sulcus, the basal surface falling over the diaphragma.

Therefore, in twenty-four of the twenty-five bodies tabulated the basal surface of the optic chiasma was located over the diaphragma sellae and the dorsum sellae. Reference to the tables will show that the portion of the chiasma located over, but not necessarily in contact with, the diaphragma sellae varies. Most frequently there is a small portion of the basal surface (approximate average of 1.5 mm.) of the chiasma which projects behind the dorsum sellae, the remaining portion resting upon the dorsum sellae and variously projecting forward over the diaphragma sellae. The degree of extension over the diaphragma, of course, is dependent upon the size (sagittal diameter) of the chiasma, the thickness of the dorsum sellae and its degree of development and forward tilt and the distance between the anterior border of the chiasma and the tuberculum sellae; that is, whether the chiasma is pre- or postfixed. Occasionally the intracranial segment of the optic nerve is so long and the junction established so far posteriorly that no portion of the chiasma is in relation with the diaphragma sellae and the hypophysis cerebri, the chiasma being located wholly upon and behind the dorsum sellae. Witness, for example, postmortem observation R.

POSTMORTEM OBSERVATION	OPTIC NERVE				OPTIC CHIASMA		
	Intracranial segment				Diameter		Location and relations
	Length		Diameter		Sagittal plane	Frontal plane	
	R	L	R	L			
A	13	13	6	5.5	10	14	Anterior edge 12 mm. behind limbus and 4 mm. behind tuberculum sellae; 9 mm. of sagittal diameter is over diaphragma sellae and 1 mm. rests upon dorsum sellae; 5 mm. intervene between chiasma and diaphragma sellae.
B	7	7	5	4	6	14	Anterior edge 8 mm. behind limbus and 2 mm. behind tuberculum sellae; 3 mm. of sagittal diameter rests upon diaphragma sellae, 2 mm. upon dorsum sellae and 1 mm. located behind the dorsum sellae; chiasma and diaphragma in contact.
C	12	12	4	4.5	7	13	Anterior edge 8 mm. behind limbus and 4.5 mm. behind tuberculum sellae; 3 mm. of sagittal diameter is over diaphragma sellae and 2.5 mm. rests upon dorsum sellae; very little space between chiasma and diaphragma.
D	4	4.5	3	4	7	11	Anterior edge 1 mm. behind limbus, the sulcus chiasmatis being entirely absent; 4 mm. of sagittal diameter is over diaphragma sellae and 3 mm. rests upon dorsum sellae; 4 mm. intervenes between chiasma and diaphragma sellae.
E	10	10	4	4	5	9	Anterior edge 10 mm. behind limbus and 5.5 mm. behind tuberculum sellae; 2.5 mm. of sagittal diameter of chiasma is above diaphragma sellae and 4 mm. from it, the remaining portion rests directly upon dorsum sellae.
F	9	8	4.5	3	8	11.5	Anterior edge 5 mm. behind limbus and 3 mm. behind tuberculum sellae; half of sagittal diameter of chiasma is over but fully 4 mm. from the diaphragma sellae and the remaining portion rests directly upon dorsum sellae.

POSTMORTEM OBSERVATION	OPTIC NERVE				OPTIC CHIASMA			Location and relations
	Intracranial segment				Diameter			
	Length		Diameter		Sagittal plane	Frontal plane		
	R	L	R	L				
G	7	8	3	3	6	8	Anterior edge of chiasma 6 mm. behind limbus and 3 mm. behind tuberculum sellae; the chiasma in its sagittal diameter rests equally upon the diaphragma sellae, the dorsum sellae and behind latter.	
H	8	8	3.5	4	7	10	Anterior edge 6 mm. behind limbus, and 3 mm. behind tuberculum sellae; the greater portion of the chiasma is located above the diaphragma sellae and 5 mm. from it, the remaining portion rests upon an elongated dorsum sellae.	
K	11	12.5	4	4	8	12	Anterior edge or border of chiasma 8 mm. behind limbus and 6 mm. behind tuberculum sellae; 3 mm. of sagittal diameter of chiasma rests upon diaphragma sellae, 2 mm. upon dorsum sellae and 3 mm. behind the latter.	
L	14	10	3	3	7	8	Anterior edge of chiasma 11 mm. behind limbus and 5 mm. behind tuberculum sellae; but 1.5 mm. of sagittal diameter of chiasma rests over diaphragma sellae and 2 mm. from it, 3 mm. upon dorsum sellae and 2.5 mm. behind the latter.	
M	4	4	5	5	5	8	Anterior edge 3 mm. back of limbus and 2 mm. in front of tuberculum sellae; approximately half of the sagittal diameter of the chiasma is located in the optic groove (sulcus chiasmatis) and the other upon the diaphragma sellae.	
N	7	8	5	5	7	10	Anterior edge or border 5 mm. back of limbus and 3 mm. back of tuberculum sellae; greater portion of chiasma rests upon and is in direct contact with diaphragma sellae, remaining portion on dorsum sellae.	

POSTMORTEM OBSERVATION	OPTIC NERVE				OPTIC CHIASMA		
	Intracranial segment				Diameter		Location and relations
	Length		Diameter		Sagittal plane	Frontal plane	
	R	L	R	L			
O	9	12	3	2.5	6	11	Anterior border 10 mm. behind limbus and 5 mm. behind tuberculum sellae; center of optic chiasma upon dorsum sellae with equal portions in front and back of this point; in contact with diaphragma sellae.
Q	5	6	3	3	5	9	Anterior border 5 mm. behind limbus and on a plane with the tuberculum sellae, hugging it closely; entire chiasma is located above diaphragma sellae, however 10 mm. intervene between the structures, spongy arachnoidal tissue filling in the interval.
R	17	16	4	3.5	5	9	Anterior border of chiasma is located 15 mm. behind the limbus and 10 mm. behind the tuberculum sellae; no portion of chiasma being in relation with the diaphragma sellae, but resting on the dorsum sellae and behind this point.
S	10	10	4.5	4	7	10	Anterior border 11 mm. back of limbus and 4 mm. back of tuberculum sellae; chiasma rests upon and is in contact with diaphragma.
T	11.5	11	3	4	4	12	Anterior border 13 mm. behind limbus and 6 mm. behind tuberculum sellae; greater portion of chiasma rests over diaphragma and in contact with it.
U	7	5	4.5	4	6	12	Anterior border of chiasma 3 mm. behind limbus; optic groove stands in vertical plane in front of chiasma; chiasma rests equally upon and in contact with diaphragma sellae, dorsum sellae and behind latter.

POSTMORTEM OBSERVATION	OPTIC NERVE				OPTIC CHIASMA		
	Intracranial segment				Diameter		
	Length		Diameter		Sagittal plane	Frontal plane	
	R	L	R	L			
						Location and relations	
350	7	7	5	4	7	14	Anterior border 10 mm. behind limbus and 5 mm. behind tuberculum sellae; greater portion of chiasma located over diaphragma, however 5 mm. intervene between them.
237	10	10	4	4	7	10.5	Anterior border 7 mm. behind limbus; optic groove stands in vertical plane 7 mm. in front of chiasma; greater portion of chiasma rests on dorsum sellae, remaining portion on diaphragma sellae.
270	10.5	11	3	4	7	13	Anterior border 10 mm. behind limbus and 4 mm. behind tuberculum sellae; chiasma rests over diaphragma sellae (not in contact) and dorsum sellae.
312	9	10	4.5	4	8	11.5	Anterior border of chiasma 9 mm. behind limbus and 5 mm. behind tuberculum sellae; chiasma over diaphragma sellae and dorsum sellae, fully 5 mm. intervening between diaphragma and chiasma.
315	8	8	5	4	6.5	10	Anterior border 8 mm. behind limbus and 2 mm. behind tuberculum sellae; chiasma and diaphragma in contact.
183	9	11	5	4	7	11	Anterior border 9 mm. behind limbus and 5 mm. behind tuberculum sellae; chiasma rests upon diaphragma sellae and dorsum sellae.
336	8	9	2.5	2.5	8	9	Anterior border of chiasma 8 mm. behind limbus and 3 mm. behind tuberculum sellae; chiasma rests wholly upon diaphragma sellae and is in contact with it.

APPLICATION

The foregoing discloses the significant fact that in 96 per cent of the bodies examined, the optic chiasma was located either wholly or partly over the diaphragma sellae and the underlying hypophysis cerebri. In 79 per cent of these, the anterior and greater part of the chiasma had the diaphragma-hypophysial relation, the dorsal part projecting variously over and behind the dorsum sellae. In 12 per cent the entire chiasma rested over the diaphragma and subjacent hypophysis. In 5 per cent the dorsal part of the chiasma rested over the diaphragma, the anterior part resting upon the chiasmatic sulcus. In 4 per cent of bodies the entire optic chiasma was located behind the diaphragma sellae and the underlying hypophysis, resting upon the dorsum sellae and projecting behind it.

The optic chiasma is, therefore, so located in the vast majority of cases that pressure or stretching of the cross fibers would appear inevitable in tumors of the hypophysis cerebri, providing, of course, the hypophysial growth is sufficiently large and progresses toward the chiasma. The typical ocular changes would, of course, be bitemporal. The chiasmal ends of the optic nerves, likewise, may be affected, especially the more medial and central fibers. Of course, the latter would, in essence, be the same fibers continued into the chiasma. It is possible for the optic nerve of one side to be more extensively involved, leading to a varied eye picture.

The specific relationship, in the individual case, of the basal surface of the chiasma to the diaphragma and hypophysis is variable and may account for variations in signs and symptoms in hypophysial disorders. For example, where the chiasma is located wholly behind the diaphragma it would appear possible for a hypophysial growth of considerable size to find its way anterior to the chiasma and between the optic nerves without causing pressure or much stretching of the cross fibers. The same, in a measure, applies to those cases in which but a small portion of the basal surface of the

chiasma is in front of the dorsum sellae. Indeed, at operation or postmortem examination it might occasionally be difficult to decide whether the elongation of the optic nerves was normal for the individual or whether it was secondary, the result of the hypophysial tumor.

The size of the angle at the junction of the optic nerves with the optic chiasma also has some bearing. While, in a general way, it is true that when the intracranial segment of the optic nerves is long and the chiasma formed far back over the diaphragma and the dorsum sellae the angle is acute, and when the intracranial segment of the optic nerve is short the angle is wide, blunt and often open U-shaped, still this is by no means always the case. Even with very long intracranial segments of the optic nerve and postfixation of the chiasma, the nerve-chiasma angle may be widely open and U-shaped, owing to the fact that the optic nerves are less convergent as they approach the chiasma. This results in a much larger space in front of the chiasma and between the optic nerves. The size of the chiasma in its transverse diameter has an important bearing in this connection.

Again where a portion of the basal surface of the optic chiasma rests upon the chiasmatic sulcus in front of the hypophysial fossa, a varied space may exist behind the optic chiasma and between the anterior portions of the optic tracts. Here one might have pressure on the optic tracts and on the dorsal portion of the chiasma. According to the series of bodies studied, this relationship is rare. However, the condition and possibilities should be remembered.

DISTANCE BETWEEN THE SELLA DIAPHRAGMA AND THE BASAL SURFACE OF THE OPTIC CHIASMA

In the accompanying charts and illustrations it will be noted that the cisterna chiasmatis, the space between the basal surface of the optic chiasma and the upper surface of the diaphragma and hypophysis cerebri varies from a potential cleft (actual contact of parts) to a vertical interval of 10 mm. Strictly speaking, of course, the actual membrane that forms

the immediate limits of this space is arachnoid, the lower part in actual contact with the diaphragma. In a large number of cases considerable enlargement, more than doubling in

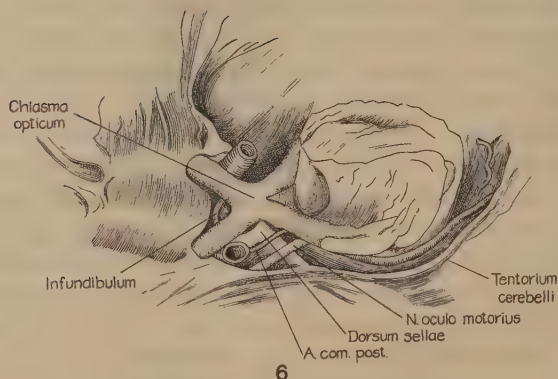
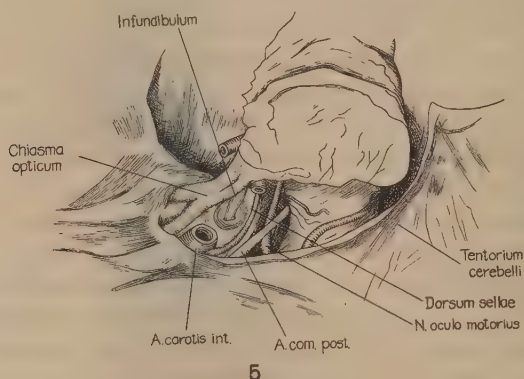


Fig. 5 Note the relatively great distance between the basal surface of the optic chiasma and the superior surface of the diaphragma sellae, indicated by the length of the infundibulum.

Fig. 6 The anterior cranial fossa is low, the dorsum sellae relatively high, resulting in a bending of the optic pathway at the chiasma, the basal surface of the chiasma and the diaphragma are considerably apart.

some instances, of the hypophysis would be required before pressure or stretching of the chiasmal fibers could be argued as the underlying factor in ocular changes.

The extent of the vertical diameter of the space in question is dependent upon a number of factors, among which may be mentioned the depth of the hypophysial fossa and size of the contained hypophysis cerebri, the degree of vertical growth of the dorsum sellae, the growth in height of the presphenoid, the level of the optic foramina, the height of the brain stem above the tentorium cerebelli, etc. When the anterior cranial fossa in the neighborhood of the presphenoid is relatively low and the brain stem simultaneously elongated above the tentorium cerebelli, the optic nerves proceed from the optic foramina obliquely dorsalward and upward to the chiasma, and the optic tracts proceed relatively far above the tentorium to their nuclei of termination.

Those who claim that pressure and stretching of the optic chiasma in hypophysial tumors always is the cause of the eye changes will find themselves in difficulty when they attempt to explain early eye changes in cases where the optic chiasma is located far above the diaphragma; that is, where eye changes occur before pressure can possibly be a factor.

THE HYPOPHYSIAL FOSSA AND THE DIRECTION OF GROWTH OF HYPOPHYSIAL TUMORS

The hypophysis cerebri is located within a fibro-osseous space—the hypophysial fossa. This is limited behind by the dorsum sellae, laterally by a heavy fold of dura mater stretching between the anterior, middle, and posterior clinoid processes within which is the cavernous sinus, and in front by the tuberculum sellae. The floor and anterior wall of the hypophysial fossa bear a varied and very commonly intimate relation to the sphenoidal sinuses. As the dura mater passes forward from the free summit of the dorsum sellae, it divides, the ectal layer lining the fossa and the ental layer forming the diaphragma sellae. In addition, one finds other perihypophysial tissues and perihypophysial spaces, suggestive of an extension of the arachnoid and pia and the subdural and subarachnoidal spaces along the infundibulum and around the hypophysis. Further study in this connection is contemplated.

The shape and differentiation of the hypophysial fossa varies considerably within certain limits. The depth is the most variable of its three dimensions. When the fossa is shallow, often with an anterior wall almost wanting and the dorsum sellae poorly differentiated, a growing hypophysial tumor could more readily expand in all directions. On the

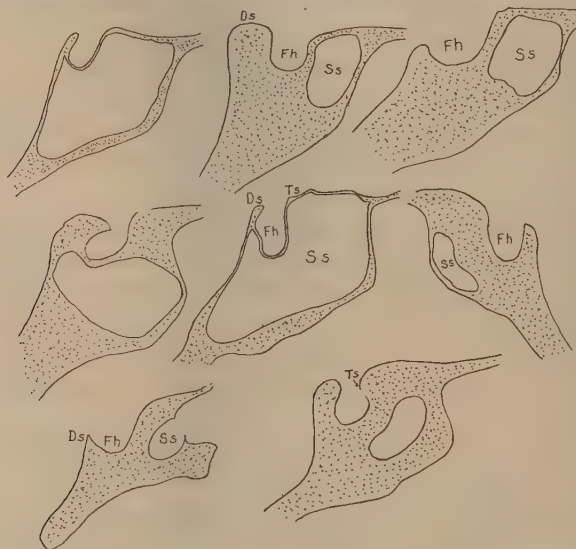


Fig. 7 Sagittal sections through the region of the sphenoidal sinus, hypophysial fossa, tuberculum sellae, and dorsum sellae. The anatomic types indicate how variations in morphology may influence the direction of growth of an enlarging hypophysis; in some cases the sphenoidal sinus may be encroached upon, in others, owing to a small sphenoidal sinus and a widely open hypophysial fossa, the growth would be directed against the under surface of the optic chiasma and the overlying brain. *Ds*, dorsum sellae; *Ts*, tuberculum sellae; *Fh*, fossa hypophyseos; *Ss*, sinus sphenoidalis.

other hand, when the dorsum sellae with its posterior clinoid processes is much elongated and bent forward, overhanging the hypophysis, and simultaneously the anterior wall of the fossa is relatively low, as is not infrequently the case, one would be led to believe that hypophysial tumors would primarily be directed upward and forward.

It would appear, however, that tumors of the hypophysis more commonly enlarge and project backward and erode the dorsum sellae and the projecting posterior clinoid processes. Naturally, one wonders why this is so, since the dorsum sellae frequently is a relatively heavy quadrilateral plate of bone. Is it possible that the course of direction of the infundibulum is a factor in determining the direction of growth of a hypophysial tumor? That is, does the infundibulum act as a stimulus, or guide, directing many hypophysial tumors to grow dorsalward? Indeed, the majority of infundibula as they leave the hypophysis are directed posteriorly and superiorly beneath and in contact with the chiasma, to reach the floor of the third ventricle.

When the optic chiasma is located wholly over the diaphragma, the infundibulum approaches more nearly the vertical. In a prefixed chiasma (rare), the infundibulum leaves the hypophysis relatively far back and courses upward and forward to its postchiasmal position.

Traquair cautions that:

It is well to bear in mind when interpreting skiagrams of suspected hypophysial or infundibular tumour that deformation of the sella with absorption of the posterior clinoids has been shown by Huer and Dandy to be by no means certain evidence of a local lesion, but a common general pressure phenomenon, especially in cases of cerebellar tumour. The trabecular or honeycomb-like shadows occasionally seen in the neighborhood of the sella turcica in transverse radiograms of the skull is due to the presence of air cells in the cellular or pneumatic type of temporal bone, which from one cause or another have been in the path of the rays passing through the sella when the photograph was taken. This shadow is sometimes mistaken for evidence of a pathological condition.

It is well to bear in mind that the dorsum sellae is extremely variable in its differentiation and anatomy. Moreover, the posterior clinoid processes may be absent altogether, that is, developmentally so.

THE DIAPHRAGMA SELLAE

The diaphragma is a small, more or less oval and horizontal fold from the inner layer of the dura mater, which roofs the hypophysial fossa and variously covers the hypophysis cerebri. An extremely variable opening, the foramen diaphragma sellae, transmits the infundibulum. The peripheral border of the diaphragma is attached to the several clinoid processes, the tuberculum sellae, the dorsum sellae, and on either side is continuous with the visceral layer of the cavernous sinus.

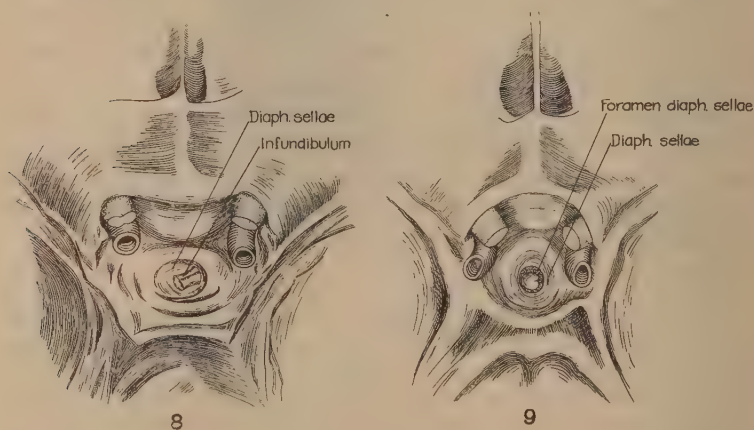


Fig. 8 Note the dense and complete nature of the diaphragma sellae. The aperture for the infundibulum is extremely small.

Fig. 9 Note the peripheral density and the enlarged central foramen for the infundibulum.

Histologically, the diaphragma sellae is a dense fibro-elastic tissue. Its ental surface has a layer of mesothelial cells which looks toward the potential space between the diaphragma and the overlying arachnoid; that is, the subdural space.

In actual practice one finds the diaphragma to vary from a very dense, strong, and, save for a very small foramen, complete roof over the hypophysis, to a mere peripheral rim, with a relatively huge infundibular foramen. In the latter cases,

the overlying arachnoid forms a loose tissue over the hypophysis within the confines of the diaphragmal foramen. Again, the greater portion of the diaphragma may be more or less fenestrated and of frail build.

It appears reasonable that the anatomy of the diaphragma sellae should at times influence the direction of growth of a hypophysial tumor. When it is frail or largely absent, the hypophysis can readily expand toward the optic chiasma. On the other hand, should the diaphragma be exceptionally

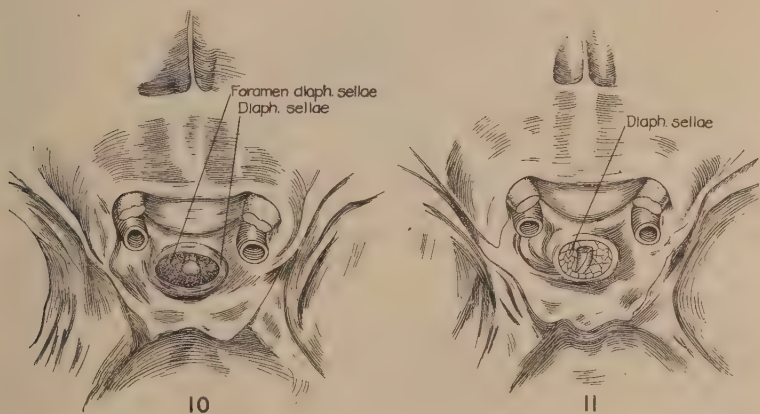


Fig. 10 Note the excessively large foramen in the diaphragma sellae. The diaphragma is represented by a mere peripheral ring of dense tissue.

Fig. 11 The diaphragma sellae is of frail build and of a fenestrated nature.

strong and complete (save for its small infundibular aperture), and the sphenoidal sinus simultaneously have pneumatized extensively in front of and beneath the hypophysial fossa, reducing its osseous walls to a papery delicacy, it would appear reasonable to expect a hypophysial tumor to expand in the direction of the sphenoidal sinuses. This might lead to delayed ocular changes, constitutional symptoms antedating them.

In those cases in which the sphenoidal sinuses have not pneumatized beneath the sella turcica, leaving the body of

the sphenoid here solid, much expansion of a hypophysial tumor in this direction would appear unlikely.⁴

Where the diaphragma over the hypophysis cerebri is very strong and complete, one would expect headache early in hypophysial tumors and the symptom to be lessened where a large opening exists in the diaphragma, since nature in a sense has done a decompression, thus relieving tension.

THE INFUNDIBULUM

As stated in the foregoing paragraph, the infundibulum varies in its course or direction from the hypophysis to its postchiasmal connection. When the optic chiasma is wholly over the diaphragma, the infundibulum is more or less vertical, and, depending upon the nearness of the basal surface of the chiasma to the diaphragma, is short or relatively long (representing 12 per cent of bodies). Occasionally the optic chiasma is prefixed, that is, rests in part upon the chiasmatic sulcus, with the result that the infundibulum courses from the hypophysis upward and forward to a position behind the chiasma (representing 5 per cent of bodies). However, in the vast majority of bodies (79 per cent in this series) the optic chiasma is postfixed, that is, is located over or rests upon the diaphragma sellae, the dorsum sellae, and beyond. Occasionally, no portion of the chiasma is located over the diaphragma (representing 4 per cent of bodies).

Therefore, in 83 per cent of the bodies examined the infundibulum extended from the hypophysis upward and dorsal-

⁴It was intended to include in this discussion an analysis of a study of the sphenoidal sinuses in fifty bodies (100 sinuses) recently examined. However, space forbids more than a brief statement. In the vast majority of bodies the sphenoidal sinuses came into very intimate relationship with the anterior wall of the hypophysial fossa. Rarely were the sinuses so diminutive that a relatively thick mass of bone intervened between them and the hypophysial fossa. In approximately half of the bodies did one or both sphenoidal sinuses project well beneath the hypophysial fossa and not infrequently was the pneumatization so extensive that the floor and anterior wall of the hypophysial fossa were reduced to extreme delicacy. It was found that a median sagittal section is altogether misleading in judging the relations of the paired sphenoidal sinuses to the hypophysial fossa. Not infrequently one sinus is small and the other excessively large. Asymmetry of the intervening septum is commonplace.

ward to its postchiasmal attachment, and in doing so cut across the basal surface of the optic chiasma in the midsagittal plane. The degree of intimacy between the infundibulum and the chiasma is dependent upon the nearness of the chiasma to the diaphragma and the dorsum sellae. In many cases the infundibulum actually molded the basal surface of the chiasma.

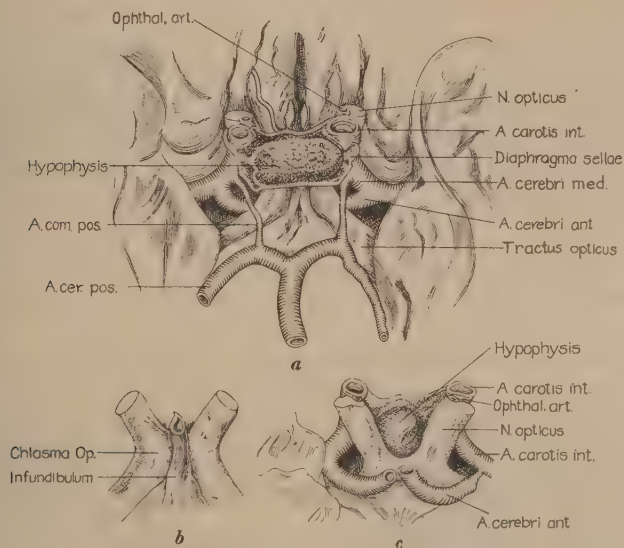


Fig. 12 A dissection of the base of the brain, showing the circle of Willis, the hypophysis, the infundibulum, and the optic pathway. A, as viewed from below; B, detail from A, showing how the infundibulum cuts the optic chiasma from before backward and in the midsagittal plane; C, as viewed from above.

It would, therefore, appear that in enlargements of the infundibulum and in many cases of the hypophysis as well, injury to the chiasmal fibers of the optic pathway would be certain. Obviously, pressure is inevitable. The common eccentric position of the foramen of the diaphragma and the hypophysial end of the infundibulum make the course of the infundibulum and the degree of intimacy between it and the chiasma somewhat inconstant. Often a large portion of the

infundibulum is visible in front of the chiasma between the optic nerves. Such infundibula are long and cross the entire sagittal diameter of the chiasma. Not infrequently in normal states is the infundibulum markedly compressed between the basal surface of the chiasma and the dorsum sellae.

THE ARTERIAL CIRCLE OF WILLIS

The circle of Willis (circulus arteriosus Willisi) has the form of a heptagon. Located in the opticopeduncular space at the base of the brain, it embraces the optic chiasma, the infundibulum, the tuber cinereum, the corpora mammillaria and the posterior perforated space. It is formed, in front, by the anterior communicating artery connecting the anterior cerebral arteries of the two sides; laterally, by the internal carotids and the posterior communicating arteries connecting the carotids with the posterior cerebrals; and behind by the two posterior cerebrals which issue forth as the terminals of the basilar artery.

A tumor of the hypophysis growing brainward would, if of considerable size, be embraced by the circle of Willis acting as a constricting band. Without going into details concerning the variations of the circle of Willis, attention will be directed to two of the arteries that appear applicable in this connection.

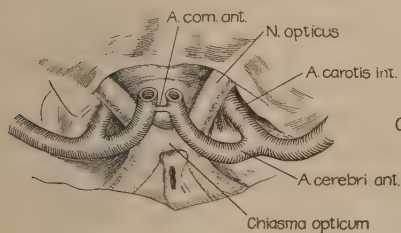
The anterior cerebral artery

The anterior cerebral arteries pass beneath and in contact with the olfactory trigone and frequently cross over the optic nerves to converge toward the beginning of the great longitudinal fissures of the brain.

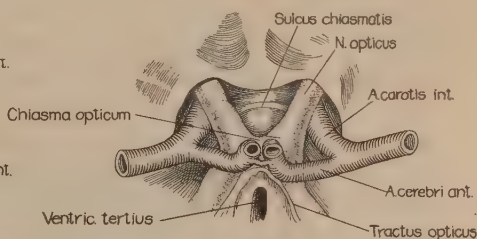
It is believed that the anterior cerebral artery where it passes over and comes in contact with the optic nerve may act as a pressure cord on the nerve in front of the chiasma in upward growths of the hypophysis and account for certain eye changes.

However, the present series of bodies showed certain very important departures from the more usual position of the anterior cerebral upon the optic nerve. It was found not

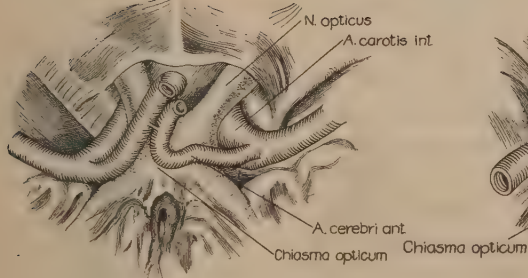
uncommon for one or the other anterior cerebral to be arched upward in the beginning of its course, then to assume a sagittal direction and cross (in contact) the optic chiasma from behind forward. In this position it would compress the crossed optic fibers if a hypophysial tumor crowded the chiasma from below. In other cases the anterior cerebrals,



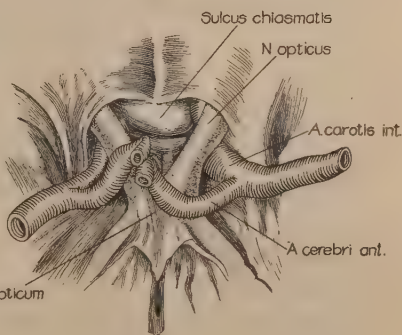
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Fig. 13 Both anterior cerebral arteries cross the optic nerves immediately pre-chiasmally in location.

Fig. 14. Both anterior cerebral arteries are so placed that pressure could readily be brought to bear upon the uncrossed visual fibers.

Fig. 15 The right anterior cerebral artery cuts the optic chiasma in the sagittal plane and the left artery has a purely optic nerve contact. It is apparent that the right artery might be a pressure cord cutting the chiasmal fibers.

Fig. 16 The right anterior cerebral artery has a chiasmal relation and the left crosses the optic nerve well in advance of the chiasma.

instead of crossing the optic nerves, rest upon the lateral aspect of the optic chiasma or even farther back upon the optic tracts and from here bend and course forward.

Asymmetry of the two anterior cerebral arteries is very common, especially as regards contacts with the visual pathway—the optic nerve, chiasma, and tract—are concerned. Just what rôle the anterior cerebral arteries play in the ocular changes resulting in hypophysial tumors is not clearly established. The fact remains, however, that the arteries frequently are of relatively large caliber and often so situated that if any pressure is brought to bear on the basal surface of the chiasma, they variously become definitive pressure cords on the several portions of the optic pathway—nerve, chiasma, and tract. The arteries of the right and left sides often do not bear the same relative relations to the optic pathway, and this might further aid in bringing about bizarre ocular changes. Reference to the accompanying drawings of dissections will clearly indicate the possibilities, when pressure is brought to bear.

The posterior communicating artery

This artery connects the posterior cerebral with the internal carotid and normally crosses the optic tract about midway and below. In this position it might be a factor in involving the optic tract in tumors pressing from below.

An important variant of this artery was encountered in this study, occurring three times in twenty-two bodies. It is illustrated in the accompanying figure 17. It will be noted that the posterior communicating comes off as usual from the internal carotid, is of unusually large caliber and very tortuous. As it approaches the region where it should join the posterior cerebral artery, it bends laterally and continues dorsally as the posterior cerebral, a small branch connecting it with the basilar artery.

The redundant portion of this artery is turned medially, and where it bends occupies a position between the hypophysis below and the optic tract above. In hypophysial tu-

mors the large artery would become caught between the tumor and the optic tract, resulting in transverse pressure upon the tract and a possible homonymous eye defect.

In the dissection herewith illustrated both posterior communicating arteries are redundant and sinuous; however, that of the right side appears more applicable.



Fig. 17 The posterior communicating arteries come off as usual from the internal carotids, but are of unusually large caliber and very tortuous. The redundant portion of the right vessel is so placed that it occupies a position between the hypophysis below and the retrochiasmal portion of the optic tract above. In hypophysial tumors the large artery would become caught between the tumor and the optic tract, resulting in transverse pressure upon the tract and a possible homonymous eye defect. *Aca*, anterior cerebral artery; *No*, optic nerve; *Aci*, internal carotid artery; *To*, optic tract; *Acomp*, posterior communicating artery; *Tolf*, olfactory tract; *Co*, optic chiasma; *Inf*, infundibulum; *Noc*, oculomotor nerve; *Acp*, posterior cerebral artery; *Ab*, basilar artery. The dotted line indicates the hypophysis and its relations.

MODE OF PRODUCTION

Morphologic

The actual mode of production of the ocular changes associated with tumors of the hypophysis cerebri is still more or less speculative. If there is but one basic factor, namely,

pressure and stretching of portions of the visual pathway by the encroaching tumor, then, at first thought, one would expect uniform eye changes. However, the eye changes are not uniform. Neither is the regional anatomy constant. Indeed, the relational anatomy of the several and fundamental segments of the optic pathway is sufficiently varied to make uniform eye manifestations highly improbable, if not impossible.

Therefore, the morphological variations, resulting in varied pressure and stretching contacts, and the bizarre eye changes are more or less in accord. Also, the more usual anatomy and the more typical ocular changes check up fairly well. It is even possible that there is a morphologic basis in those cases where in a known hypophysial tumor the eyes escaped involvement altogether. Such cases have been reported by deSchweinitz, Cushing, and others.

Apart from the varied relational anatomy of the optic pathway, deSchweinitz and Carpenter have directed attention to the fact that there may be many individual variations in the composition of the optic chiasma which could account for departures from the more usual eye picture in hypophysial tumors. Indeed, the optic nerve fibers in man rarely may suffer complete decussation in the chiasma as in many lower vertebrates. Even in a few mammals (guinea-pig, mouse) a crossing of optic fibers in the chiasma is complete. Again, in very rare instances the decussation of visual fibers in man is wanting altogether, all of the fibers passing directly to the optic tract of the same side. Such reversions would, of course, profoundly alter the more usual ocular changes in hypophysial tumors. The position of the more vulnerable fibers in the chiasma, especially the macular bundle, would be changed and pressure less liable to occur.

Despite these rare variations, one need but look into the anatomy of a large series of bodies to see that pressure and stretching of some portion of the optic pathway would be inevitable in a large number of instances should the hypophysis undergo sufficient enlargement. In some cases pres-

sure and stretching would necessarily be delayed, due to less intimate relationships.

An appreciation of the usually accepted localization of the several fasciculi of visual fibers within the optic pathway is, of course, necessary in connection with an understanding of symptoms resulting from pressure or what not on the several segments of the optic pathway. Hensen and de Vialat and Henschen made valuable contributions in this localization. There are particularly three fiber bundles to be thought of, the uncussated, the decussated, and the central or macular. Space forbids further consideration of them here.

Toxic

There are some observations that seemingly mar the absolute acceptance of the pressure and stretching theory. Among others may be mentioned the observation that ocular changes occurred before it was believed that the hypophysial tumor was sufficiently enlarged to produce pressure or stretching of the visual fibers. Also, the important observation that in the very common hypophysial enlargements during pregnancy, while there is a bitemporal contraction, indicating pressure or stretching of the chiasma, the other eye manifestations suggestive of a hypophysial tumor are wanting. Of course, it must be recalled that the enlargement of the hypophysis cerebri in pregnancy is, in all likelihood, a physiologic process and the enlargement incident to a tumor, a pathologic process. In the latter, one would expect the elaboration of toxins, in the former, not. The former apparently is needed, the latter obviously not.

These observations lend support to the toxin theory of ocular changes in hypophysial tumors. However, if the theory is acceptable, why do not all eyes, in known hypophysial tumors, show some changes? A varied anatomy or morphology could scarcely apply here. May it be, that in all cases of hypophysial tumors, there are certain early and specific ocular changes which are missed because ophthalmologists see the majority of patients too late?

If toxins are elaborated by a tumorous hypophysis, why should the optic nerve, especially certain component fibers of the chiasma, be attacked by the toxin? All we can say here is, that there must be a special affinity by these more highly specialized fibers for the specific toxin; that is, there is a selective action. The latter, of course, has been observed and established in other conditions and in other tissues.

Pathway

Comparative histologic investigations indicate that the hypophysis has a dual activity, one dependent upon the basophils, the other upon the acidophils. Tilney's studies indicate that the basophils yield their secretion by way of the residual lumen of the buccal part and the infundibular process of the neural part of the hypophysis to the cerebrospinal fluid and the acidophils directly to the blood spaces in the gland. Whether the usual metabolic products of the normal hypophysis and the toxins in a pathologic hypophysis are similarly disposed of, is not established.

In this connection it would appear applicable to discuss certain other phases in the regional anatomy. The arterial circle of Willis is located within the basal cisternae (pontis, interpeduncularis, chiasmatis). These cisternae are part of the general subarachnoidal space at the base of the brain. These spaces are more or less of a spongy nature; their compartments intercommunicate and are lined with mesothelium. The blood vessels as they traverse the subarachnoid space derive mesothelial investment on their way into the brain, chiasma, hypophysis, etc., thereby extending the subarachnoidal space in the form of perivascular spaces into the parts supplied. The perivascular spaces sooner or later lose their mesothelial wall and become continuous with the proper tissue and cellular spaces found within the several parts.

Dandy and Goetsch have shown that the anterior hypophysial lobe (in dog) receives its blood supply from eighteen or twenty small arteries which converge toward the infun-

dibulum from the various components of the circle of Willis. These vessels break up into large sinusoidal channels within the hypophysis. The veins are like the arteries in arrangement. They pass to a venous circle overlying the circle of Willis and drain into the great vein of Galen. A branch from each internal carotid joins to form a common trunk which supplies the posterior lobe. The veins here empty into the circular sinus in the diaphragma. This arrangement found in the dog in all likelihood applies to man as well.

The optic chiasma and the chiasmal end of the optic nerves receive blood supply by branches derived from the anterior cerebrals, the internal carotids, and the forward portion of the posterior communicating arteries. These vessels initially are subarachnoidal in position and invested by mesothelium. In extending to an extrasubarachnoidal position they carry the subarachnoidal space in the form of perivascular spaces into the parts supplied.

The perivascular spaces coming into direct relationship with the tissue spaces of the hypophysis would apparently make possible the passage of metabolic products, toxins, etc., directly to the subarachnoidal cisternae beneath the chiasma; that is, the cisterna chiasmatis. The latter is extremely variable, however, and at times is of conspicuous size (see elsewhere). This seems to be in keeping with the perivascular spaces of the brain which carry products of metabolism into the subarachnoidal space and there augment the amount of cerebrospinal fluid found and, moreover, change its chemistry.

Weed injected a true solution of foreign salts (potassium ferrocyanide and iron-ammonium citrate in equal parts) into the subarachnoid space in living animals. After a proper interval the tissues were fixed in an acid medium, resulting in the precipitation of the foreign salts as ferric ferrocyanide (Prussian blue). By this method which was safeguarded by proper checks, Weed demonstrated the direction of flow of the cerebrospinal fluid and its points of passage into the venous system. It would lead us too far afield and, in a

sense, be irrelevant here to enter into a discussion of his contribution. Suffice it to say that precipitation of Prussian blue "extended in the basilar spaces about the infundibulum and around the optic chiasma, to continue outward for variable distances in the subarachnoidal space of the optic nerve and more restrictedly about the olfactory nerves." Schoenberg likewise has actually seen in living dogs stain placed in the lateral ventricle and the subarachnoidal space gradually spreading into the sheaths of the optic nerves.

While not in keeping with the believed direction of flow within the brain perivascular spaces (brain toward the subarachnoid space), the extension of the blood vessels from a subarachnoidal position into the chiasma, etc., shows the possibility of toxins within the chiasmatic cistern being carried into the extensions of the subarachnoidal space, and since the latter ultimately become confluent with the actual tissue spaces, toxins brought in contact with the visual fibers. The more highly specialized visual fibers are particularly vulnerable and would be the first to suffer.

Just what rôle the lymphatics of the dural capsule of the hypophysis play in this connection is not known. However, no proper lymphatics have been demonstrated within the central nervous system. Whether or not in pathological states there is a passage of toxins from the perihypophysial spaces to the subdural space immediately over the hypophysis and from there through the arachnoid to the cisterna chiasmatis over the hypophysis is not established. The fact, however, remains that the foramen in the diaphragma sellae frequently is very large, allowing the subarachnoidal spaces to come into intimate relationship with the hypophysis and the perihypophysial tissues within the aperture of the diaphragma. Altered pressure, that is, hyper- or hypotonic conditions on the two sides of the arachnoid (subdural and subarachnoid), may be an important factor, as Weed has clearly shown in another connection.⁵

⁵ Elsewhere in this study mention is made of the perihypophysial tissues and spaces and that they are suggestive of an extension of the three cerebral meninges and the meningeal interspaces along the infundibulum and around the hypophysis. Absolute proof of such continuity, however, was not established at the time of

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completing copy of this paper (March, 1923). Since then Dr. Walter Hughson, Johns Hopkins Medical School, appears to have definitely established that the meninges bear the same relationship to the hypophysis that they do to the brain proper (personal communication from Prof. Lewis H. Weed, under date of May 1, 1924). Hughson was able to inject the perihypophysial subarachnoidal space by means of injections under high pressure, or by means of preliminary shrinkage of the brain by hypertonic solution. This would provide a direct pathway and would preclude the necessity of toxins passing through the arachnoid.

A NEW METHOD FOR THE MICROSCOPIC STUDY OF LIVING GROWING TISSUES BY THE INTRO- DUCTION OF A TRANSPARENT CHAMBER IN THE RABBIT'S EAR

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Transparent living tissues, thin enough to transmit sufficient light for microscopic observation, have been widely used by anatomists and pathologists for many years in the study of cell growth and behavior. The classical object has been the transparent tail of the amphibian larva, from which has been gained much of our present knowledge of the growth and reactions of blood vessels, lymphatics, nerves, connective-tissue cells, and wandering cells. To a considerable extent, also, the web of the frog's foot has been used. While many facts of fundamental importance and wide application have been discovered, still the question frequently arises whether there may not be differences in the growth and behavior of mammalian, as compared with amphibian cells and tissues.

The only translucent regions in mammals adaptable for microscopic study are the omentum and mesentery. These have been used, but their availability is greatly limited, owing to the necessity of anesthetizing the animal and to the inflammation which is produced by the unusual exposure. The few hours' period during which such studies may be continued is too short to permit of observations on growth processes.

During the past sixteen years living tissues have been studied by numerous investigators, by employing the 'tissue culture' method, invented by R. G. Harrison ('02). With this method, however, the tissues are entirely removed from

the body, and the growth changes which take place diverge greatly from the normal.

The desire to obtain a region in which the growth and behavior of living mammalian tissues could be satisfactorily studied microscopically led to an attempt to devise a new method. The suggestion came from the classical glass-chamber method of E. Ziegler, introduced in 1875. As employed by E. Ziegler and others, particularly A. Maximow ('02), this method consists of the construction of a chamber, made from two cover-glasses fastened together with a very thin space between them. This chamber was placed under the skin or between muscles and left for varying lengths of time. The space between the cover-glasses was invaded by cells and tissues, including wandering cells, fibroblasts, blood capillaries, etc., and, by removing the chambers at intervals, the observer was able to study the progressive changes in the fixed and stained specimens. Maximow also used celloidin chambers, which, after removal, were imbedded and sectioned. Immediately after the removal of the glass chambers, he made observations on the living cells, but was unable to keep them alive longer than an hour and a half, owing to the cutting off of the blood supply in the removal.

The problem, then, became one of putting the chamber in a location in which it would be accessible for microscopic observation, while still in position in the animal. Briefly, it was found entirely feasible to install the chamber as a double-walled window in the rabbit's ear. In developing the method, the attempt was first made, after sealing the chamber on three sides, to shove the open side under the skin through an incision made in the edge of the ear, so that the chamber would project from the side. Chambers so placed soon became loose and dropped out. Next was tried the method of cutting a hole in the midst of the ear and tucking all four sides of the chamber under the skin. This method, after several attempts, proved successful. Ordinary cover-glasses were tried in the construction of the chambers, but they were found to be too fragile. A very good substitute was dis-

covered in isinglass, which, in spite of the presence of lines and scratches which are sometimes difficult to distinguish from living structures, makes a fairly satisfactory chamber. It has the advantage of elasticity and strength, may be easily pierced for anchorage holes, and may be split to any desired thickness.

Two general methods have been used for obtaining growths of living tissues in the chambers. One consisted of the insertion of a preformed chamber, into which the cells might grow, the other involved the enclosing of a thin strip of tissue already formed, and containing circulating blood vessels, between the two walls of the chamber. The construction and insertion of the preformed chambers was carried out as follows: Two pieces of isinglass $10\ \mu$ to $15\ \mu$ thick were cut into squares measuring 2 cm. $\times$ 2 cm. and holes large enough to admit a sewing needle were punched in the corners of each piece. Beside each hole, on one of these pieces, a tiny glass block, which had been cut from a no. 1 cover-glass, was fastened to the isinglass with fairly thick balsam. The piece was then quickly flamed once or twice to harden the balsam. Following this, a very small amount of balsam was placed on top of each block, and the other piece of isinglass, which also had been sterilized by flaming, was laid over the block, care being taken to see that the holes were exactly opposite each other. In this way a chamber was formed, open on four sides, having a thickness equal to that of a no. 1 cover-glass plus the thickness of the balsam. A final flaming completed the construction of the chamber and made it ready for insertion into the tissues of the ear. In choosing the site for operation, it was found best to select a place where the ear was most nearly flat, avoiding the large artery, which passes up the center, and the large veins, which course down both margins of the ear. The ordinary precautions to insure asepsis were employed. Having produced local anesthesia by subcutaneous injection, around the site of the incision, of a 1 per cent solution of procaine to which had been added adrenalin chloride, a square incision,

slightly smaller than the dimensions of the chamber, was made through the skin and connective tissue down to the cartilage. These two layers of tissue were stripped off and discarded. A probe was then passed under the skin around all the free edges of the wound, to allow ample space for the chamber. As soon as all haemorrhage was controlled—usually slight pressure is sufficient—the chamber was filled with physiological salt solution, slipped into position, and the edges of the skin pulled over its borders, covering, also, the holes. Each corner was anchored with silk thread, the needle passing down through the entire ear, including the holes, and back again through the tissues beyond the chamber. The ear was then turned over, and the lower layer of skin and the cartilage, covering the underside of the chamber, were removed by another square incision. It was found that a clot, resulting from a small amount of bleeding around the free edges of the wound where the skin overlaps the borders of the chambers, is advantageous, as it cements the skin to the isinglass. This is an important factor in that it adds to the life of the chamber.

The second method was as follows: The construction of the chamber was the same, except that the second side of the chamber was not cemented on until the time of the operation. The square incision was made as before, but passing through only the layer of skin, which was stripped off. The edges of the skin were then retracted. This exposed the connective-tissue layer with its blood vessels and nerves. One half of this tissue was removed down to the cartilage. The remaining strip of connective tissue was probed under and a space made beneath the edges of the skin as in the first method. One of the pieces of isinglass, with the corner blocks already mounted, was slipped partly under this strip of tissue, which covered one half of the pieces of isinglass. Two holes were pierced in the strip of tissue to allow two of the blocks to come through. Thick balsam was then dropped on each block, and the other piece of isinglass laid over them—thus sealing the chamber, which included the preformed tissues.

After removing the skin retractors, the chamber was anchored and the tissue removed from the underside of the ear, as in the first method.

By this second method living tissues were made accessible for microscopic study and new growths into the unoccupied space of the chamber could be watched from the very beginning. While this method proved very satisfactory for the study of numerous problems, it is desired to obtain an even thinner growth within the window, in which it will be possible to observe more clearly individual cells. It is planned to use for this purpose a raised table, fastened to one side of and occupying only a part of the chamber, which shall leave a thinner observation space than has yet been feasible.

In both types of chamber air was excluded by filling the chamber with sterile physiological salt solution.

Once implanted, the majority of the chambers have remained in place for periods varying from a week to two months without requiring any particular precautions. There has been a tendency for the skin to retract on one or two sides of the chamber after two or three weeks. Since this has occurred on the convex side of the ear, it is believed that this difficulty can be obviated by placing a flat double frame of aluminum outside the chamber.

For microscopic observation, the rabbit is placed on its back, the feet tied, and the head held in place by a wooden collar and trough. The ear is lightly clamped in position over a glass slide, held by a mechanical stage. The rabbit, in this position, remains quiet for hours and observations may be made day after day for weeks.

It is beyond the scope of this article to discuss the cell processes which may be, and to some extent have already been observed in these chambers, other than to mention briefly what may be seen and to point out some of the possibilities. In the preformed chambers there is seen for a number of days a fibrillar network, probably consisting of fibrin. This appears as early as the second day. At this time there are groups of erythrocytes interspersed here and

there through the network. Other regions remain cell-free until later. By the end of the first week the meshes of the fibrillar network become heavier. There are few erythrocytes—unless a fresh haemorrhage has occurred—and the scattered groups which at first appeared have now lost their deep coloring for a light shade of pink. Various other types of cells appear, among which are connective-tissue cells and wandering cells. Some of these are caught in the fibrillar network, others are floating freely in the fluid between the meshes, and still others flatten themselves out on the walls of the chamber, and are continually changing their shape and position from day to day. At this time, also, a rather sharply outlined mass of erythrocytes, lying 1 or 2 mm. from the visible edge of the chamber, may be seen, and they usually indicate the presence near by of circulating capillaries. With the high-power lens, these erythrocytes seem to be in definite rows, as if they were lying in channels. In a day or two this mass extends farther from the edge, and circulating capillaries become visible. On the first appearance of this new tissue the transparency is dimmed, on account of the abundance of dilated, newly formed capillaries packed with erythrocytes. As time goes on, however, the picture becomes clearer in places and structures stand out distinctly. The endothelium with its nuclear thickenings, individual cells of the blood, and such phenomena as Krogh's 'plasma skimming' may be easily seen.

Of approximately ten preformed chambers which have been inserted, two have shown new-formed circulating blood capillaries, one of the two remaining intact for a month and a half. In some cases the material between the fibrillae remains fluid, in others it has a consistency which prevents cells from being pushed about mechanically.

The most interesting chamber thus far has been one introduced by the second method, in which a thin layer of already formed tissue was left in one half of the chamber. This was implanted about three months ago and is still connected, although part of it has worked free of the ear. This speci-

men was, for the first two weeks, rather opaque, owing to erythrocytes which entered at the time of operation. It gradually became more and more transparent, until it showed with great clearness arterioles, capillaries, and veins, the endothelium standing out with great clearness. It is believed that already it has provided the best experimental field in a mammal for watching the changes in endothelium. Moreover, there occurred, from the edge of the tissue, considerable new formation of capillaries, while on the under surface of the isinglass in the unoccupied part of the chamber new cells grew and wandered, and their changes were watched from day to day.

The possibilities of the method are numerous. The ability to see individual cells growing and moving about while living and growing in their natural fluid environment furnishes a field for carrying out studies somewhat similar to those of tissue cultures. Also, the opportunity is afforded to study the part which these various cells play in the formation of new tissue, in phagocytosis, and in other reactions connected with function and growth, in determining the mode of growth of blood capillaries, lymphatics, nerves, etc., in a mammal, many of which phenomena have been observed and described in the tadpole's tail and the frog's web.

The studies are yet in their infancy. Definite plans are being made for perfection of the method. The results already obtained, however, seemed to justify an early publication of the method, on account of the promising possibilities.

I am deeply indebted, and wish to acknowledge my gratitude to Dr. E. R. Clark, in view of his invaluable suggestions.

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A CASE OF BONE FORMATION IN THE MEDULLA OF THE SUPRARENAL GLAND

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TWO FIGURES

Although the histology of the suprarenal is well known to every investigator, a specimen was recently obtained which showed a striking deviation from the usual structure. Upon microscopic examination of sections of a monkey's suprarenal, there were definite and unmistakable evidences of bone formation. Since the presence of bone in this situation is unusual, a brief description seems appropriate.

The suprarenal had been removed for routine class material from a female monkey belonging to the genus *Macacus rhesus*. Sections of the organ were fixed in potassium bichromate, embedded in celloidin, stained in hematoxylin and eosin, and mounted in balsam. These preparations showed the suprarenal cortex, medulla, and bone in sharp differentiation.

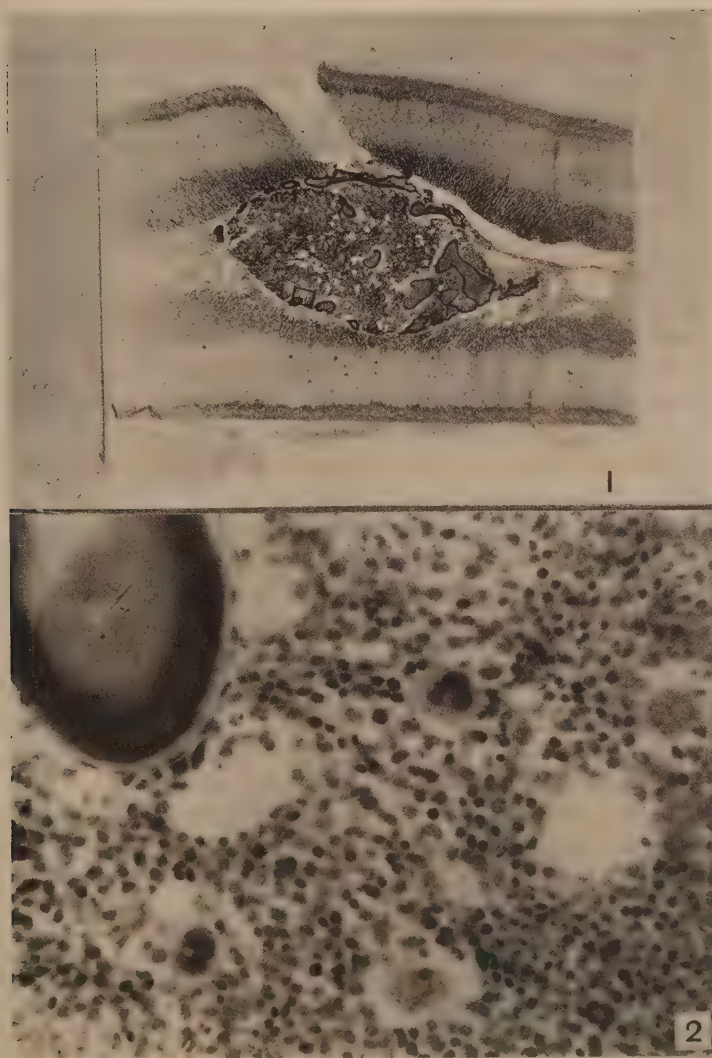
The area of bone was elliptical in form. It occupied the central portion of the medulla, touching the cortex at two points. Interposition of medullary cells at the rounded ends prevented the bone from further reaching the cortex. The relative position of the formation is shown in figure 1 ($\times 16$). Osseous spicules lay scattered throughout the region. The bone-marrow was typical in that it contained an average number of megakaryocytes in a field of myelocytes and fat-cells. These giant cells (fig. 2, $\times 400$) with their annular contour and lobulated nucleus were in all respects similar to giant cells in normal bone-marrow. Again, Howship's

lacunae, cavities enveloping the osteoclasts, were manifest in many of the bone structures. Most interesting was the regular outline of a definite periosteum circumscribing the entire area. With this sharp margin encircling the bone, there arose a distinct contrast to the regular suprarenal tissue. Failure of the bone to appear in every section indicated that the formation did not extend throughout the gland. The organ was indeed normal in all respects except for the presence of bone in the medulla.

Besides typical bone and marrow in the section, there were blue-stained areas of calcification. Although bone formation in the suprarenal is without precedent, calcification has already been observed there. Through the courtesy of Doctor Wislocki of this department a section of a cat's suprarenal, containing calcified areas, was examined: both calcification and ossification may therefore occur in the suprarenal. But the explanation of bone in such a site is far more difficult, for calcification can be considered a late stage of tissue degeneration.

In their studies on the cerebrospinal fluid of cats, Cushing and Weed observed numerous instances of calcification and ossification in the arachnoid. The calcium depositions were in non-vascular areas, for the nutritive exchanges of the arachnoid are derived from cerebrospinal fluid rather than circulating blood. But in every case the bone deposits were vascularized. This is a fundamental point that receives further substantiation from the finding of bone in the suprarenal. They concluded that "calcification and ossification depend on some underlying cause, primarily or secondarily, accompanied by proliferation of mesothelial cells."

The most promising explanation for this appearance of bone involves the embryology of the organ with a possible perversion of development. Embryologically, from the mesoderm arise the locomotive tissues of the body—muscles, bones, ligaments, and connective cells, together with the circulatory and mobile systems, the heart, blood vessels, blood cells, and varied moving tissue cells. Particularly that



Figures 1 and 2

element of the mesoderm forming vessels, blood, connective tissue, and mobile cells is given the name mesenchyme.

The cortex of the suprarenal is also derived from mesoderm, arising by the invagination of coelomic mesothelium. Buds from the proliferation of these mesothelial cells penetrate the mesenchyme beside the aorta. Later they lose their serosal attachment and blood vessels ramify through their structure. For some time the zona glomerulosa suffers suspended development and the complete specialization of the cortex reaches a late maturity. The medulla is rich in blood vessels, the chromaffin tissue derived from the sympathetic nervous system resting upon an extensive network of sinuses. Certainly, the prolific vascular bed with its blood vessels throughout and the late development of the organ make possible such perverted growths of bone.

Though mesoblastic cells manifest a fair degree of specificity, which differentiates them in structure and activity, they often betray extraordinary powers of taking new forms and functions. Bone formation especially involves varied interrelations and modifications of connective tissue. Through the activity of osteoblasts, which are specialized connective-tissue cells, bone may be constructed from fibrous tissue and cartilage. Since bone was found in the medulla of the suprarenal, a locality ordinarily harboring no osteoblasts, it is suggested that near-by undifferentiated mesodermal cells have been modified to the latter cells. Or more specifically, the mesoderm of the primitive blood vessels may have formed osteoblasts instead of maturing to endothelium. With a rich capillary bed, with an abundance of mesodermal tissue at every hand, there are manifest opportunities for this event. Osteoblasts may have followed along the nutrient artery to the organ and started their work of laying down bone. Whether by simple infiltration through the blood stream or by modification of other mesodermal cells, it is the presence of the osteoblasts which makes possible bone formation. It is evident that the surrounding tissue and especially the circulatory system make their presence no difficult matter.

Though it can be scarcely more than suggested, the absence of cartilage cells would seem to indicate a membrane ossification. It may readily be that layers of bone, lying adjacent to the periosteum, were laid down by it. Whatever the method of ossification, however, the final picture is thoroughly typical of bone. Osseous trabeculae amidst the myeloid tissue with an enveloping periosteum are thoroughly regular features of true bone.

Though Cushing and Weed have emphasized the proliferation of mesothelial cells in their findings of calcification and ossification in the arachnoid, another factor would seem to govern the deposition of bone in the suprarenal. The presence of typical bone-marrow surrounding the osseous area introduces an additional item that indicates a close relationship with the vascular supply. Numerous cases of calcium, bone, and bone-marrow deposits have been reported in various organs (Bunting), but the manifest evidence of bone-marrow in an endocrine gland adds an interesting feature. It lends support to the already prevalent views that bone formation is linked with vascular supply.

There are, then, several possibilities to which the formation of bone in the suprarenal may be ascribed. In every instance the probable explanation can be traced to embryological development. The osseous area was found in a rich vascular bed. The arteries may have furnished the avenues of entrance into the medulla for the osteoblasts, or the vascular mesoderm may have formed osteoblasts instead of pursuing their usual bent. In any event, the late embryological development of the organ and the network of vessels seem responsible for the presence of the bone in the suprarenal. The striking feature of the specimen is the bone-marrow, which has apparently not been described previously in areas of calcification or ossification in the suprarenal and which brings good support to the argument for the embryological explanation of the abnormality. Yet the possibility of a pathological process affecting normal tissue can never be excluded.

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SUR L'EXISTENCE DE BLOCS TANNOPHILES GÉANTS, DANS LA CELLULE LUTÉINIQUE DE LA LAPINE

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PLANCHE 1 (19 FIGURES)

La méthode tanno-ferrique¹ ne colore d'habitude dans la cellule lutéinique que des granulations spéciales, occupant la zone de la sphère et que nous avons trouvées récemment dans des coupes colorées par le tannin-fer. Cette méthode est la seule qui met en évidence ces granulations, mais elle ne colore rien de plus dans la plupart des cellules du corps jaune. Cependant, quand on examine des corps jaunes vrais colorés par la méthode en question, on reste surpris de trouver dans quelques cellules, peu nombreuses, de gros blocs colorés en noir intense, présentant la forme sphérique ovoïde, carée, irrégulière ou en croissant (figs. 1 à 8). Ces blocs, visibles parfois aux faibles grossissements, sont isolés dans la cellule; d'habitude, on n'en voit qu'un seul, logé quelque part. Une des caractéristiques dominantes des blocs en question est la dimension parfois énorme qu'ils présentent; on en voit qui ne sont pas plus grands que le nucléole des cellules lutéiniques, mais d'autres atteignent les dimensions du noyau et plus encore (fig. 4). Les blocs qui revêtent la forme d'un croissant, d'un gros trait, etc., sont, dans la réalité, des

¹ A. L. Salazar. Méthode de coloration tanno-ferrique. *Compt. Rend. Soc. Biol.*, T. 83, p. 1655. 1923, La méthode tanno-ferrique; mordantage tanno-acétique. *Anat. Rec.*, vol. 26, no. 1. 1923, La méthode tanno-ferrique; mordantage à chaud. *Compt. Rend. Ass. Anat.*

masses sphériques avec une grosse vacuole: on voit la mince pellicule qui limite cette vacuole avec netteté.

Dans des cas très rares on voit des cellules avec deux ou trois blocs énormes, sans noyau visible et cytoplasme plus ou moins coloré: ce sont probablement des cellules en dégénérescence. D'ordinaire, les cellules, où l'on trouve les blocs tannophiles, sont en tout identiques aux autres cellules lutéiniques: elles ne présentent ni dans le cytoplasme ni dans le noyau le moindre signe de dégénérescence.

Les blocs en question ne se colorent pas par la laque ferrique après le Bouin ou après chromisation en Kolster, ni par les autres méthodes usuelles: jusqu'ici, nous n'avons vu ces formations qu'avec le tannin-fer après fixation dans la liqueur de Bouin.

Il est actuellement impossible de comprendre la signification exacte de ces formations: on peut affirmer cependant qu'elles évoluent et se transforment. La forme en croissant est due à une vacuolisation des blocs; la substance qui occupe dans le vivant ces vacuoles, de nature probablement lipoïde, croît au dépens de la substance du bloc, qui s'épuise graduellement.

Cette évolution présente une analogie frappante avec ce que nous avons décrit sous le nom de 'chondriome tannophile'² dans la cellule interstitielle: l'évolution, au point de vue morphologique, est identique, la coloration spécifique par le tannin-fer après fixation en Bouin est aussi un caractère commun. Nous rappellerons à ce propos qu'en décrivant le chondriome tannophile nous avons signalé deux variétés de cellules; les unes chargées d'une foule de petits blocs, les autres avec (en général) un seul bloc énorme, atteignant souvent les dimensions du noyau; celles-ci sont plus rares que les autres. Or, il existe une analogie frappante entre ce dernier type et l'aspect des blocs que nous sommes en train de décrire: chez la cellule lutéinique, comme chez la cellule interstitielle à gros blocs, nous voyons des blocs géants solitaires, tantôt sphériques, tantôt en croissant.

² A. L. Salazar. Le chondriome tannophile lipogène des cellules interstitielles de l'ovarie de la lapine. *Compt. Rend. Soc. Biol.*, 1921, T. 2, p. 604.

Malgré ces similitudes frappantes, nous ne pouvons affirmer qu'il s'agisse de substances de composition et fonction similaires; c'est-à-dire, nous ne savons encore si on peut considérer ces blocs comme un chondriome tannophile lipogène. Nous ne savons même si dans la glande interstitielle les gros blocs solitaires, qu'on voit dans certaines cellules, sont absolument identiques à la constellation de petits blocs, qu'on voit dans les autres. Il est à remarquer que les gros blocs solitaires se voient dans les cellules plus jeunes, la constellation de blocs petits dans les cellules plus avancées; que les cellules interstitielles à gros blocs sont relativement rares, les cellules à petits blocs assez fréquentes; que les cellules à gros blocs sont en général solitaires, les autres, à petits blocs, réunies en nappe étendue; mais, d'un autre côté, on trouve parfois, quoique rarement, de gros blocs parmi la constellation de petits blocs et des types cellulaires intermédiaires. De sorte que la question n'est pas claire et on reste indécis; dans la cellule lutéinique, l'indentité d'évolution et de réaction chromatique suggèrent l'homologie avec le chondriome tannophile, la rareté de ces formations, peu en harmonie avec une fonction générale de la cellule, ne s'accorde pas bien avec cette interprétation. Tandis qu'entre la constellation de petits blocs et le chondriome de la cellule il existe des rapports manifestes, nous n'avons jamais observé la moindre relation entre les gros blocs et les éléments mitochondriaux; or, il en est de même pour les blocs géants lutéiniques. L'analogie existante entre les gros blocs lutéiniques et les gros blocs de certaines cellules interstitielles est donc assez marquée; de sorte que, ou ces dernières sont cellules à chondriome tannophile, et alors on doit considérer les blocs des cellules lutéiniques comme étant une variété de chondriome tannophile, ou elles ne le sont pas, et alors il est probable que les blocs dont nous nous occupons ne sont pas eux aussi homologables au chondriome tannophile.

Certains faits semblent indiquer que ce chondriome est une manifestation de dégénérescence de la substance mitochondriale, c'est-à-dire, une dégénérescence physiologique ou

involution qui aboutit à la formation de substances lipoïdes. Si la cellule lutéinique subit une involution définitive, cette hypothèse est très plausible; si elle ne subit qu'une involution temporaire et cyclique, l'hypothèse en question est encore admissible, mais il est vrai que dans ce dernier cas la différence entre un processus sécrétoire et une involution cyclique est un simple jeu de mots.

En somme, nous ne possédons pas actuellement des données suffisantes pour ébaucher une hypothèse à propos de toutes ces formations; les quelques faits intéressants, que nous avons observés à ce propos, ne sont pas encore établis avec une extension suffisante pour servir de base à une interprétation.

Dans les coupes traitées par le tannin-fer on observe quelques cellules lutéiniques présentant des formations complexes dont les rapports avec les blocs géants ne sont pas certains: les figures 10, 11, 12, 13, 14, 15, 16, 17, 18 représentent quelques-unes de ces cellules. Dans la figure 14 on voit un bloc ovoïde en tout analogue au bloc tannophile qu'on voit dans la même cellule, mais coloré en gris; nous ignorons s'il s'agit d'un bloc de même nature, mais avec des affinités chromatiques plus faibles, ou d'une formation différente.

Dans la figure 15 on voit un corps ovoïde au centre de la cellule, coloré en gris sombre, ayant inclus de petites masses noires.

Dans la figure 16 trois formations analogues entourent le noyau; deux sont colorées en gris-noir, avec des masses noires, l'autre est claire, semée de granulations, tannophiles. La figure 17 représente une formation que nous avons trouvée jusqu'ici une seule fois: une masse spongieuse, grise, entourant le noyau en croissant. Dans la figure 18 on voit deux cellules: dans une de ces cellules on voit une grosse lacune entourée d'une masse colorée en noir, dont les bras, après avoir entouré la lacune, s'estompent graduellement et passent par des transitions insensibles à l'aspect du cytoplasme: c'est-à-dire, à l'une des extrémités de la cellule, le cytoplasme présente une intense réaction tannophile autour d'une lacune.

Dans la figure 19, enfin, on voit deux blocs élégamment dessinés en gris et noir. Les formations dessinées dans les figures 15, 16, 17 n'ont pas, croyons nous, des rapports avec les blocs géants; celles des figures 18 et 19, sont, au contraire probablement des blocs dégénérés ou modifiés par les réactifs.

Une autre catégorie de formations est celle que se trouve représentée dans les figures 10, 11, et 12. Il s'agit d'un système de lacunes et de vacuoles, tantôt périphériques (fig. 11), tantôt centrales (fig. 10 et 12), parfois ayant les mêmes dimensions (fig. 11) mais le plus souvent formant un système constitué par une vacuole plus grande entourée ou suivie d'autres plus petites (fig. 10 et 12). Chaque vacuole du système est entourée d'un cortex coloré en noir, épineux, irrégulièrement épais. Il est probable, quoique nous n'ayons pas de preuves certaines, que les systèmes en question dérivent de la vacuolisation d'un bloc géant. La figure 9 semble en fournir une preuve; nous y voyons un bloc en croissant en rapport avec un système de vacuoles, quoique, dans ce cas, il s'agisse d'un système en communication avec l'extérieur ou avec un canalicule venant de l'extérieur et pénétrant dans la cellule. Si entre les figures 9, 10 ou 12 il y avait des rapports certains, le bloc géant serait un plaste élaborant une substance versée par la cellule dans les espaces intercellulaires, probablement lymphatiques. Mais si, par hasard, il n'y a pas de rapports entre la figure 9 et la figure 10 ou 12, il n'en est pas moins certain que dans le cas de la figure 9 il s'agit d'un bloc tannophile et que ce bloc élabore une substance que nous voyons en train d'être versée dans l'extérieur.

Il reste le cas de la figure 13; il s'agit certainement d'une cellule en dégénérescence. La réaction tanno-ferrique colore beaucoup de substances provenant de la dégénérescence de certains éléments, comme la pellucide, la membrane de Slanjansky, l'oocyte: dépendant on ne peut pas savoir s'il s'agit de la désintégration d'un bloc géant ou d'une coloration cytoplasmique de désintégration.

Nous voyons, en résumé, que dans le métabolisme de la cellule lutéinique des plastes tannophiles interviennent, élab-

orant par métamorphose directe, des substances qui sont versées dans l'extérieur soit après transformation complète du bloc géant, soit au fur et à mesure de la transformation. Cette transformation des plastes se révèle cytologiquement par la perte de leur tannophilie, et par la vacuolisation. Cette intervention des plastes tannophiles se fait pendant l'âge jeune et adult du corps jaune vrai; plus tard ils disparaissent: il s'agit donc d'un processus caractéristique de la cellule lutéinique jeune en rapport avec une élaboration à fonction inconnue de la cellule en question. Mais nous ignorons la nature de la substance dont sont constitués les blocs, et leur origine. En effet, une des caractéristiques de ces blocs est leur apparition brusque; jamais nous n'avons pu observer des faits qui puissent être rapportés à une génèse de leur substance; s'il est vrai que certains blocs sont plus petits, et qu'il semble qu'on puisse les considérer comme des blocs jeunes, il est vrai aussi que ces blocs petits présentent la même coloration noire, les mêmes formes en croissant, en anneau, etc., indiquant une transformation: en tout, ces blocs petits se comportent comme les blocs géants, et ils ne peuvent être considérés comme des formes jeunes. Quelle est donc l'origine de ces formations? Certainement, si dans les coupes colorés au tannin-fer, ils apparaissent brusquement dans la cellule, c'est qu'il y a des formes jeunes que la réaction en question ne révèle pas. Mais l'emploi d'autres méthodes n'a pas permis de trouver un rapport quelconque entre ces blocs et les autres formations connues de la cellule lutéinique; c'est là un problème cytologique à résoudre.

PLANCHE

PLANCHE 1

EXPLICATION DES PLANCHES

1, 2, 3, 4, 5, 6, 7, 8 Divers aspects des blocs géants dans les cellules lutéiniques du corps jaune vrai de la lapine. Bouin, tannin-fer. Oc. Comp. 4, Reichert. Objc. imm. $\frac{1}{12}$, Leitz.

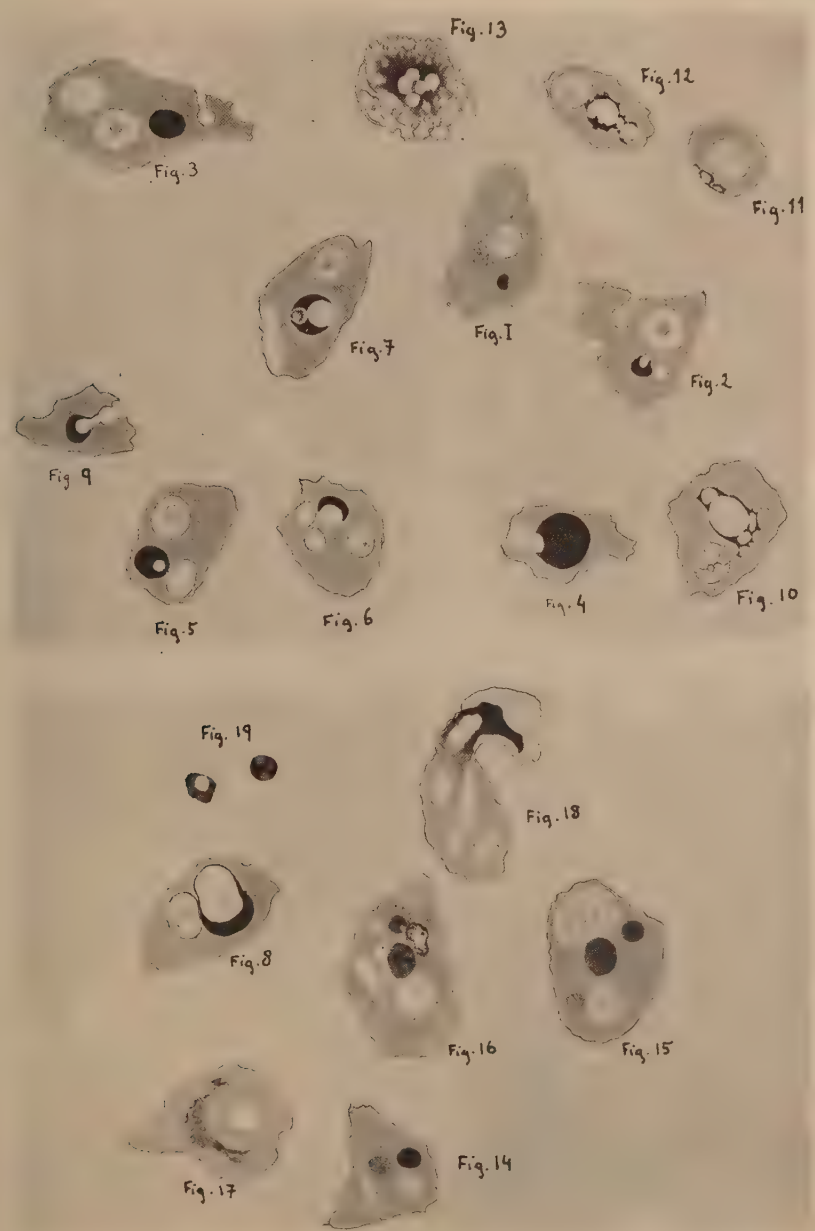
9 Bloc géant en communication avec une série de vacuoles s'ouvrant dans l'extérieur de la cellule. Idem.

10, 11, 12 Cellules présentant un système de vacuoles dont la paroi est constitué par une substance tannophile (métamorphose des blocs géants?). Idem.

13 Cellule en dégénérescence tannophile. Idem.

14, 15, 16, 17, 18 Cellules lutéiniques présentant diverses formations colorées par le tannin-fer, à signification inconnue. Dans la figure 14 on voit à côté d'un bloc géant, coloré en noir, un bloc ayant la même forme, mais coloré en gris. Idem.

19 Blocs avec des vacuoles clairs et gris; probablement blocs géants modifiés par les réactifs. Idem.



LA COLORATION NUCLÉAIRE ET DE FOND DANS LES COUPES TRAITÉES PAR LE TANNIN-FER

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La méthode tanno-ferrique¹ imaginée par nous pour l'étude de certaines questions de l'histologie de l'ovaire est une méthode très spécialisée à cause du nombre très restreint de formations qui se colorent. Dans la cellule ce nombre est encore plus restreint; dans l'ovaire, par exemple, le chondriome tannophile de la cellule interstitielle, les amas tannophiles et le deutoplasme de l'oocyte sont les seules formations qu'on trouve colorées dans les cellules. Dans une coupe bien réussie, ni les noyaux ni les cytoplasmes ne se colorent et les formations tannophiles se dessinent en noir encre de Chine sur un fond blanc. D'habitude, étant donné le caractère très spécialisé de la méthode, ce que suppose son application à un objet bien connu, cette absence de coloration nucléaire et de fond ne gêne pas, elle est plutôt favorable car elle simplifie la préparation. Cependant en certains cas, quand on a besoin d'établir des points de repère, d'étudier des rapports, de voir l'aspect des cellules, etc., elle rend difficile l'observation: une coloration nucléaire et cytoplasmique est alors utile. Or, après l'action successive du tannin et du fer les colorations habituelles ou bien n'ont plus de prise sur la coupe, ou donnent des résultats qui s'écartent de ceux qu'on désire. Colorons par exemple une coupe au tannin-fer, faisons ensuite agir la safranine aniliné: le

¹ A. L. Salazar, Méthode de coloration tanno-ferrique, *Compt. Rend. Soc. Biol.*, T. 83, p. 1655. La méthode tanno-ferrique: mordantage tanno-acétique. *Anat. Rec.*, vol. 26, no. 1, 1923. La méthode tanno-ferrique; mordantage à chaud. *Compt. Rend. Ass. Anat.*, 1923.

résultat qu'on attend, la coloration nucléaire, n'est pas obtenu. Car, dans ces circonstances la safranine, au lieu de colorer les noyaux, fait vivre la coloration et teinte uniformément de rose le fond : la coupe prend un aspect qui rappelle certaines méthodes à l'or. En outre elle différencie la préparation, car la safranine, suivant la plus ou moins grande affinité qu'elle possède pour les éléments tannophiles, déplace plus ou moins vite la coloration noire. Du reste si l'on laisse agir ce colorant peu de tempts on obtient une différenciation avec coloration rose du fond. Il arrive quelque chose d'analogue avec d'autres colorations ; avec l'acide picrique, par exemple, il n'y a pas de virage, mais il y a différenciation et substitution chromatique. Dans ces circonstances, c'est-à-dire, après l'action successive du tannin et du fer, nous n'avons obtenu quelque résultat qu'avec le picro-carmin de Ranvier ; il ne colore pas les noyaux, mais donne au fond une coloration jaunâtre-ôcre agréable.

Mais si, au contraire, on fait agir les colorants nucléaires et cytoplasmiques avant le tannin et le fer, la coloration se fixe sur les points désirés, et la réaction tanno-ferrique s'ajoute à celle des autres colorants. On peut ainsi colorer les noyaux à l'hématéine, à la thionine, etc. ; cependant tous les colorants ne donnent pas des résultats également heureux, non seulement à cause des combinaisons chromatiques, mais parce que quelques uns nuisent un peu à la réaction. D'après nos essais, la coloration qui réussit mieux est celle qu'on obtient avec la safranine aniliné ; si l'on désire seulement colorer les noyaux on fait agir, après la safranine, le tannin-fer ; si, outre la coloration nucléaire, on désire une teinte de fond, on traite les coupes, après la safranine, par la picro-fuchsine de Van-Gieson ou Hensen, et ensuite par le tannin-fer. Cette coloration ainsi combinée, safranine picro-fuchsine-tannin-fer, donne des coupes très belles, avec une grande variété de tons, et des combinaisons chromatiques intéressantes.

Les noyaux sont colorés en rouge safranine, les cytoplasmes en jaunâtre ; les éléments qui sont exclusivement fuchsi-nophiles en rouge-fuchsine ; ceux qui sont exclusivement tan-

nophiles, en noir; ceux qui sont à la fois tannophiles et fuchsinophiles en violet plus ou moins rouge, plus ou moins foncé selon l'équilibre des affinités; enfin ceux qui sont à la fois tannophiles et avides d'acide picrique, restent en gris verdâtre ou en vert, ou en noir-verdâtre. Les tons sont assez purs, brillants, et transparents, de sorte que cette combinaison est utile pour l'analyse topographique et chromatique. Le tannin-fer, ainsi combiné, peut servir de base à une méthode de coloration des plus polychromatiques et d'un emploi non plus spécialisé mais général.

La technique est facile; si la pièce a été fixée correctement, si elle n'a pas été chauffée excessivement pendant l'inclusion, ou au moment du collage, etc.; si en un mot, les conditions nécessaires pour la réussite de la méthode tanno-ferrique ont été réalisées, il est facile de réussir aussi la coloration combinée. Quelques minutes pour obtenir une forte coloration à la safranine, lavage à l'eau; ensuite on traite par le tannin; c'est le moment délicat car le tannin agit à la fois comme différenciateur et comme mordant: il différencie la safranine-picro-fuchsine et sert de mordant au sel ferrique. Or il faut que ces deux actions soient à la fois suffisantes et non excessives; c'est un moment de la technique où il faut tâtonner. Après l'action du tannin on lave à l'eau largement, on traite ensuite par le fer, etc. Si on désire aussi une coloration de fond, on fait alors agir après la safranine, la picro-fuchsine, et ensuite le tannin, puis le fer.

Voici le résumé technique:

1. Fixation en liquide de Bouin;
2. Inclusion en paraffine à une température aussi basse que possible;
3. Coupes au microtome et collage sur lame, en évitant soigneusement un chauffage excessif;
4. Surcoloration à la safranine anilinée;
5. Lavage à l'eau distillée;
6. Picro-fuchsine de V. Gieson pendant quelques minutes;
7. Lavage à l'eau distillée;

8. Différentiation et mordantage dans un bain récemment préparé de tannin-acétique ainsi composé: tannin, 6 gr.; acide acétique, 10cm³; eau distillée, 30cm³. Les coupes abandonnent de nuages de couleur sous l'action du tannin qui différencie la safranine et la picro-fuchsine; en même temps il se produit le mordantage nécessaire pour l'action du fer;

9. Lavage à l'eau distillée;

10. Bain d'alun de fer à 4 pour cent;

11. Lavage à l'eau distillée; alcool à 90°, absolu, xylol;

12. Montage en baume salicylé.

LES VAISSEAUX ET LES LACS SANGUINS DANS L'HYPOPHYSE HUMAINE (LOBE GLANDULAIRE)

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TROIS FIGURES

Dans l'hypophyse du fœtus à terme on trouve de nombreux vaisseaux de différents calibres et quelques-uns présentent des irrégularités dans leur lumen parce qu'ils sont obligés de décrire de capricieuses sinuosités et doivent s'adapter aux cordons des cellules glandulaires à épaisseur variable.

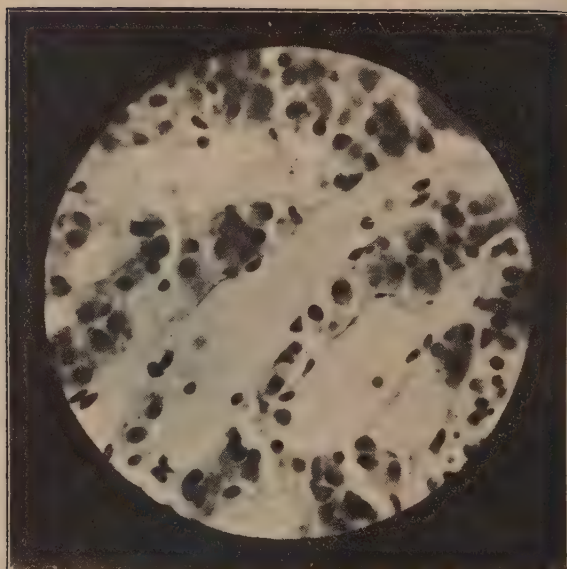
Le lobe glandulaire du fœtus à terme est si riche en vaisseaux que l'on trouve dans quelques régions alternativement une couche de cellules et un vaisseau, de telle façon que l'on y voit une file de cellules entre deux vaisseaux sanguins.

Quoique, suivant mes observations sur l'hypophyse du chien adulte que j'ai déjà publiées,¹ j'ai insisté sur sa richesse vasculaire, j'ai depuis constaté que le lobe antérieur du fœtus à terme est incomparablement plus riche.

J'ai aussi coupé des hypophyses du coq, du dindon, de la souris, du lapin, du cobaye, du mouton, d'un enfant âgé de 7 ans et d'un homme, et je n'ai jamais vu une relativement aussi grande superficie de vaisseaux que celle trouvée dans le fœtus (voir les microphotographies).

Dans ce dernier j'ai remarqué quelques lacs sanguins dont un était de dimension exagérée par rapport aux autres (microphotographies).

¹ Portella, A., 1918. L'hypophyse a l'état normal, *Anais Scien. da Fac. Med. do Porto*, vol. 3, no. 4, e IV, no. 1.



1



2

Fig. 1 Abondants vaisseaux de l'hypophyse du fœtus à terme, oc. 3, obj. im. $\frac{1}{12}$.

Fig. 2 Grand lac sanguin de l'hypophyse du fœtus à terme, oc. 3, obj. 3.

En comparant la superficie vasculaire de l'hypophyse du fœtus à terme, de l'enfant âgé 7 ans, de l'homme de 25 ans et de la femme de 65 ans, nous pouvons admettre que l'hypophyse augmente au volume par prolifération cellulaire, soit par le processus de division indirecte, soit (rarement) par division directe, comme je l'ai déjà vu dans le lobe glandulaire du chien.

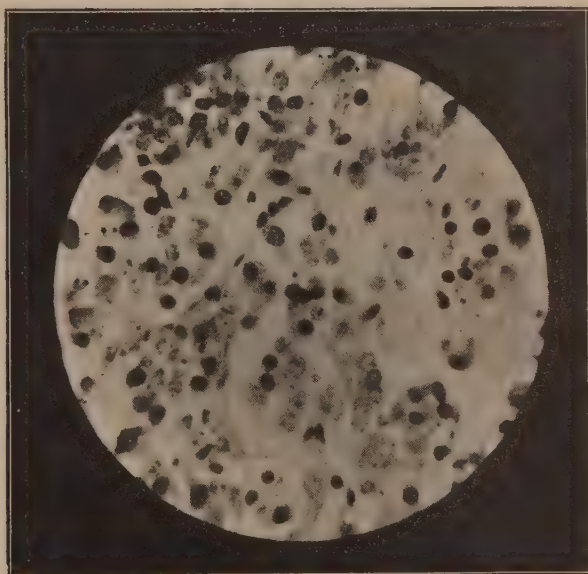


Fig. 3 Vaisseaux de l'hypophyse d'un enfant âgé de 7 ans, oc. 3, obj. im. $\frac{2}{12}$.

Pendant que la richesse vasculaire est établie dès le commencement, il n'y a pas de néoformation de vaisseaux après le développement structural de l'hypophyse. Les cordons glandulaires deviennent toujours plus forts à mesure que les animaux avancent en âge.

À mesure que l'hypophyse croît, les cellules envahissent les lacs sanguins, de sorte que ceux-ci diminuent en grandeur absolue et relative.

(Travail du Laboratoire de Physiologie de la Faculté de Médecine du Porto)

LE LOBE ANTÉRIEUR DE L'HYPOPHYSE DU FOETUS À TERME

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UNE FIGURE

Dans l'hypophyse du foetus à terme nous n'avons pas remarqué des manifestations abondantes de l'activité granuleuse comme dans l'hypophyse des animaux en voie de croissance extrautérine. Dans l'organe d'un enfant âgé de 7 ans nous voyons des cellules en abondance qui se colorent par l'éosine et dont le protoplasme ne fixe pas l'hématoxiline ferrique, mais nous voyons aussi de nombreuses cellules, à grains nettement séparés, de grandeur variable, avec leurs noyaux en divers états d'activité, comme je l'ai déjà vérifié dans l'hypophyse du chien.¹

Le mécanisme de la sécrétion dans l'hypophyse humaine paraît analogue à celui qui s'opère dans l'hypophyse du chien, et toutes les phase d'activité sécrétoire se retrouvent dans le lobe glandulaire de l'enfant âgé de 7 ans.

De même, les lacs colloïdes provenant de la dégénérescence d'une cellule centrale s'observent aussi chez l'enfant, et je crois que ces lacs sont destinés à recevoir les sécrétions des cellules environnantes qui ne peuvent pas se mettre en communication avec un vaisseau sanguin et que plus tard, par suite de la dégénérescence d'une de ces cellules en couloir, s'établit la liaison entre le dépôt colloïde et le vaisseau. Je crois que par suite de ce double mécanisme, c'est-à-dire par suite de la formation de lacs colloïdes et de la dégénérescence des cellules adjacentes en couloir, se forment les processus

¹ Portella, A., 1918. L'hypophyse à l'état normal. Anais Scien. da Fac. Med. do Porto, vol. III, no. 4, e IV, no. 1.

permettant l'entrée de la colloïde dans le courant circulatoire, comme je l'ai déjà fait remarquer dans une communication antérieure.²

Les grains à sécrétion passent, par refoulement des cellules actives, dans l'espace creusé entre les cellules, où ils fusionnent et prennent ensuite les caractères chimiques de la colloïde en présence des couleurs, suivant mes observations

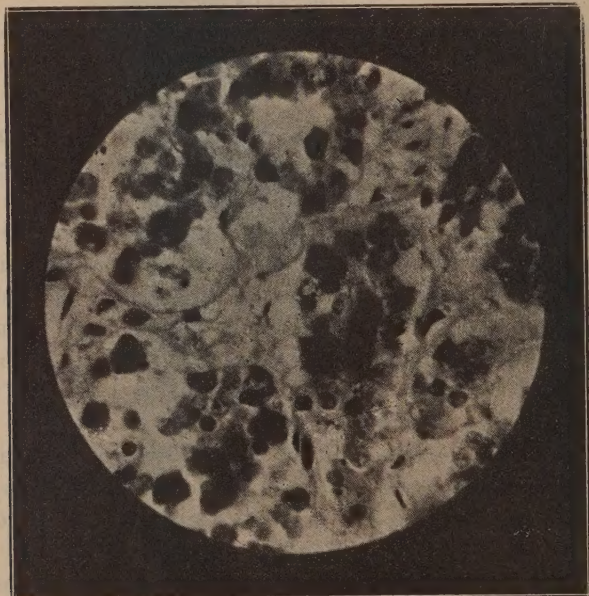


Fig. 1 Lobe antérieure de l'hypophyse de l'enfant âgé de 7 ans. Oc. 3, obj. $\frac{1}{12}$ in. Dans un des lacs colloïdes on voit une masse siderophile (en noir) provenant de la secretion.

nombreuses; ou alors les grains passent directement dans les espaces lymphatiques et traversent ensuite les vaisseaux, soit à l'état de grains soit après solubilisation, comme je l'ai déjà démontré.

Il est probable que les lacs colloïdes ou les espaces colloïdes constituent des réserves pour être utilisées au moment opportun.

² Portella, A., 1919. *Ergastoplasma e Condrioma*. Idem, vol. III, no. 1.

Dans l'hypophyse du fœtus à terme nous ne trouvons pas de cellules dégénérées ni les abondantes lacs colloïdes comme dans l'hypophyse du chien.

J'explique ces faits précisément par la richesse vasculaire et par le fait que dans l'hypophyse du fœtus les cellules sont en étroit voisinage avec les vaisseaux; d'ailleurs les cellules de l'hypophyse du fœtus n'ont pas besoin d'un travail intense comme c'est le cas chez les animaux pendant la vie extra-utérine.

Il est démontré que l'hypophyse de la mère augmente, pendant la gestation, en poids et en volume et présente tous les caractères d'un organe en suractivité,³ et cela explique le petit nombre de cellules à grains que l'on trouve dans l'hypophyse du fœtus, puisque les glandes endocrines de la mère suppléent celles du fœtus.

Les cellules à grains du fœtus sont parsemés dans le lobe glandulaire et ne sont pas réunies ni agglomérées comme elles se présentent dans les hypophyses des animaux jeunes ou adultes, chez qui les cellules à grains occupent la majeure partie de la masse centrale du lobe glandulaire en des amas noirs (par l'hématoxiline ferrique) tranchant sur le fond orangé des cellules colorées par l'éosine.

Mais il convient de dire que les cellules de l'hypophyse du fœtus n'ont pas une aussi grande affinité pour l'éosine que les cellules des hypophyses plus âgées. Beaucoup des cellules prennent une teinte intermédiaire entre celle donnée par l'éosine et celle par l'hématoxiline ferrique. Par ces caractères je suis amené à penser que les cellules de l'hypophyse fœtale sont aptes à commencer leur travail de sécrétion aussitôt que l'individu vient au monde, et dès qu'il ne peut plus recevoir l'influence de l'hypophyse maternelle.

³ Siguret, A., 1912. Contribution à l'étude histologique de l'hypophyse pendant la gestation. Thèse, Paris, no. 72.

Launois, 1903. Les cellules siderophiles de l'hypophyse chez la femme enceinte. Comptes rendus de l'Ass. des Anatomistes.

Thoan, 1907. L'hypophyse au cours de la gestation. Bull. de l'Acad. Roy. de Belgique, XIX.

